
**REPORT TO
THE SENATE ARMED SERVICES COMMITTEE
AND
THE HOUSE ARMED SERVICES COMMITTEE**

on

**Department of Defense
Animal Care and Use Programs 1999**

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LIST OF ACRONYMS

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care International
AALAS	American Association of Laboratory Animal Science
ACLAM	American College of Laboratory Animal Medicine
ADCS (M&RA)	Assistant Deputy Chief of Staff for Manpower and Reserve Affairs
ADCSPER	Army Assistant Deputy Chief of Staff for Personnel
AL/HR	Armstrong Laboratory/Human Resources
APHIS	Animal and Plant Health Inspection Service
ARI	Army Research Institute
ASBREM	Armed Services Biomedical Research Evaluation and Management
AWA	Animal Welfare Act
AWIC	Animal Welfare Information Center
BRD	Biomedical Research Database
CDR, AFHSD	Commander, Air Force Human Systems Division
CRISP	Computer Retrieval of Information on Scientific Projects
DDR&E	Director, Defense Research and Engineering
DoD	Department of Defense
DTIC	Defense Technical Information Center
FDA	Food and Drug Administration
FEDRIP	Federal Research in Progress
FY	Fiscal Year
GME	Graduate Medical Education
IACUC	Institutional Animal Care and Use Committee
IG	Inspector General
ILAR	Institute of Laboratory Animal Research
IRAG	Interagency Regulatory Alternatives Group
JDL	Joint Directors of Laboratories
JTCG	Joint Technology Coordinating Groups
LAM	Laboratory Animal Medicine
NHP	Nonhuman Primate
NIH	National Institutes of Health
NPRDC	Navy Personnel Research and Development Center
NRC	National Research Council
NTSC	Naval Training Systems Center

OPRR	Office for the Protection from Research Risks
OSD	Office of the Secretary of Defense
OTSG	Office of the Surgeon General
PHS	Public Health Service
PL	Public Law
POC	Point of Contact (Primary Contact)
RDT&E	Research, Development, Test, and Evaluation
S&T	Science and Technology
STRICOM	Simulation Training and Instrumentation Command
TAPSTEM	Training and Personnel Systems Science and Technology Evaluation and Management
USDA	United States Department of Agriculture
WRAIR	Walter Reed Army Institute of Research

SECTION I

INTRODUCTION/OVERVIEW

This is the Fiscal Year (FY) 1999 Report to Congress on Department of Defense Animal Care and Use Programs. In addition to a general overview, this report provides a detailed account of Department of Defense (DoD) animal use. It addresses the DoD's publicly accessible database, animal care and use oversight policies and procedures, alternatives to animal use programs, and animal use.

The report covers animal research conducted by the DoD including education, training, and testing both in DoD laboratories and by extramural projects funded by the Department for FY99. This report does not include information on animals used by the DoD solely for the purpose of food preparation for human or animal consumption, ceremonial activities, recreation, or the training, care, and use of military working animals.

I.1 REQUIREMENTS NECESSITATING THE USE OF ANIMALS BY THE DoD

DoD use of animals in research, development, education, and training is critical to sustained technological superiority in military operations in defense of our national interests. The DoD's biomedical research, development, test, and evaluation (RDT&E) training programs that are dependent upon animal use ultimately translate into improved military readiness as well as reduction in morbidity and mortality associated with military operations. These programs directly contribute to ensuring that service men and women maximize their capabilities to survive the numerous and various hazards they face around the world. We have an irrefutable moral obligation to our soldiers, sailors, airmen, and marines to provide the maximum protection and care possible. DoD researchers are committed to accomplishing this goal, and it is important to emphasize that, as in nonmilitary research programs, the involvement of animals in research cannot be avoided.

DoD research has benefited greatly from animal use alternatives such as nonliving systems, cell and tissue culture, and computer technology. However, complex human organ system interactions, in addition to environmental factors and confounding variables, necessitate the continued judicious use of animal models in DoD programs. Although many innovative animal use alternatives have been developed and are in use by Department scientists, situations remain in which there are no acceptable non-animal alternatives available. For example, there are no adequate models addressing the movement and general effects of drugs, toxicants, or pathogens in the body. Similarly, cell and tissue cultures are severely limited in their abilities to simulate endocrine, neurological, immune, or inflammatory responses. Whenever possible, the DoD will embrace new advances, technologies, and breakthroughs in animal use alternatives. The chapter on alternatives in this report gives a full account of the programs and numerous animal use alternatives implemented in DoD laboratories.

Disease remains a major cause of disability and sometimes death in military operations and conflicts. Today, humanitarian and peacekeeping operations place our troops in regions around the globe, and expose them to endemic pathogens to which their immune systems are naive. Soldier health and performance can be compromised by a variety of diseases for which there are no effective preventive or therapeutic countermeasures. Research toward the development of effective pretreatments and therapies can only be accomplished with the help of specific animal models that support pathogens under study. For example, the life cycles of malaria pathogens require multiple host organ systems, precluding the exclusive use of *in vitro* research studies.

During operations Desert Storm and Restore Hope, outbreaks of respiratory diseases, diarrheal diseases such as shigellosis, and parasitic diseases such as leishmaniasis and malaria, threatened the health and well-being of our troops. Indeed, the DoD is still assessing and addressing concerns over the long-term effects of various environmental, physical, and medical factors associated with the Persian Gulf Conflict. It is obvious that the health and well-being of military personnel extend far beyond the immediate scope of the battlefield.

One of the most critical areas requiring DoD animal use is the compelling need to develop vaccines, drugs, and therapies to protect, sustain, and treat service men and women during military operations. These are needed for protection against numerous militarily relevant diseases and threats, many of which can result in potentially fatal diseases or conditions that have no known treatments, therapies, or cures. Ethical concerns, as well as regulatory requirements of the Food and Drug Administration (FDA), necessitate that candidate vaccines and drugs be demonstrated safe and efficacious in laboratory animal models prior to initiation of human use protocols whenever possible. The rationale for this is to prevent the fielding and use of ineffective or dangerous treatments. Drug efficacy screens are generally conducted at the lowest possible phylogenetic level, in rodents. Given that drug response is often species-specific, promising drugs are subsequently tested in nonhuman primates. During the final stages of vaccine and drug development, large-scale safety and efficacy testing is usually conducted using human volunteers.

The DoD must develop the materiel and technological means to provide critical and immediate battlefield injury care to service men and women. This is often provided by field medical personnel in an austere, harsh, and hostile environment, hours away from a definitive care hospital, unlike medical counterparts found in civilian emergency medicine and trauma management. A domestic, low velocity projectile gunshot patient in a modern civilian shock and trauma center will be supported and resuscitated by a full complement of medical staff with a plentiful supply of oxygen, fluids, medications, surgical intervention, and nursing. The combat casualty may be supported by only a single aidman and the medical supplies, experience, and expertise he can carry. No *in vitro* model can simulate the range of effects of multiple organ failure or shock that so often follows physical trauma.

There are numerous research areas, including medical chemical and biological warfare defense, where animal-based studies are particularly critical because, in the search for understanding and developing protection against many highly lethal agents, human use protocols are simply not possible. Ethical considerations severely restrict or preclude the use of clinical studies in this research area. The recent terrorist release of both chemical and biological agents in Japan underscores the need to develop protective medical countermeasures for both civilian and military personnel. The DoD is charged with the responsibility of identifying and developing these countermeasures to protect the nation, and carefully regulated animal studies are absolutely vital to the success of these biomedical research programs.

This responsibility of the DoD to maintain the health of men and women and their families wherever they work, on bases, on the battlefield, or in peacekeeping missions around the world underlies the need for the DoD to conduct research, and to train and educate military health care providers. Clinical investigation programs at Medical Treatment Centers support postdoctoral Graduate Medical Education (GME) programs, in which physicians receive residency training in special areas such as pediatrics, orthopedics, surgery, and emergency critical care. To be certified, the GME programs must demonstrate that a Medical Center has programs to provide research opportunities for both staff and students. These clinical investigation programs provide training in research, protection of human subjects, and use of animals in research, and provide opportunities not only for staff and GME students, but for patients who desire to participate in research protocols, such as Multicenter Oncology and Pediatric Oncology protocols. In this regard, Congress has mandated that the DoD will work closely with the National Institutes of Health (NIH) to provide more opportunities for DoD beneficiaries to participate in the NIH-sponsored protocols. Many of the clinical investigation training protocols, such as surgical skills training for

microvascular or reproductive surgery, support GME programs that follow requirements set by the American College of Surgeons. These courses provide essential opportunities for the training of medical personnel who will work in both military and civilian sectors. Programs using animals for GME training are subjected to veterinarian oversight and are conducted in the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) accredited facilities.

The use of animals is also important in the DoD's nonmedical programs. These studies include the development of biological sensors, sonar, echolocation, biorobotics, aviation construction materials, and hearing and eye protection systems. There are also nonmedical studies to understand learning and memory physiology in an attempt to model the brain's circuitry for advanced data processing computers and robotic machinery. These advanced computers and robots will eventually reduce the risk that our service men and women encounter in their daily duties. The DoD performs marine biology research to better understand the military working marine mammals. In addition, the marine mammals are investigated to determine their auditory detection thresholds in marine use as sentries. Studies of biosonar systems are conducted to enhance the use of military marine mammal systems for mine detection and retrieval, personnel detection, and reconnaissance.

I.2 BENEFITS OF ANIMAL RESEARCH

The requirements enumerated in [Section I.1](#) point to the benefits that are provided to the military working community that are derived from DoD animal use research and training. DoD laboratories and extramural contractors provide the capability to solve the medical and nonmedical problems of the future through the efforts of internationally renowned medical and scientific experts working in state-of-the-art facilities and in the field. The Department conducts or funds research, development, training, and evaluation to sustain the operational capabilities of today's service men and women. As noted in the previous section, many of these programs require the use of animals to meet their mission requirements and result in many benefits for both the military and the civilian sector ([Tables I-1 and I-2](#)). The military benefits from programs that do research in areas that currently threaten military personnel, such as combat trauma, chemical and biological agents, infectious diseases not endemic to the United States, directed energy, and occupationally unique health hazards from military operations and environmental extremes. These research programs contribute significantly to the readiness and sustainment of the DoD's warfighting capability, and focus heavily on the prevention of casualties.

Because DoD research requirements must mirror DoD research benefits to military personnel, further elaboration of military benefits noted in a short list in [Table I-1](#) and a more extensive list of specific benefits realized in FY99 is found in [Appendix A](#). These benefits reflect the diversity of DoD research efforts that were extended on behalf of the men and women in our armed forces.

It is important to recognize that DoD research requirements benefit civilians in the United States and in the world community. As noted in the previous section, the DoD is charged with the responsibility of developing countermeasures against chemical or biological agents that may be released by terrorists against civilian targets. Both classes of agents were released against Japanese civilians in crowded urban settings in 1995.

The DoD also indirectly or directly advances understanding of our knowledge of cardiovascular disease, trauma care and treatment, respiratory injuries, burns, and specific surgical procedures. The DoD's role in some of these areas is critical in that some of these areas traditionally receive only modest funding support in civilian research programs. Marine researchers and policymakers also benefit from DoD marine mammal research through its indirect contribution of a better understanding of the impact of noise pollution from ships on marine mammals.

Table I-1 Animal Use Benefits

<p>Medical</p> <ul style="list-style-type: none">FDA safety and efficacy testing in preclinical studiesVaccine development against diseases and biological agentsDrug evaluation screening studiesGulf War illness researchBasic, preclinical and clinical cancer researchIdentification and control of insect disease vectorsBioengineering artificial limb control for amputeesDeveloping noninvasive diagnostic toolsDesign and testing of drug delivery systemsIdentifying countermeasures for hemorrhage and shockCharacterizing health effects of occupational exposure to toxicantsDetermining the basic biology of adult respiratory syndromeDetermining the health effects of embedded munition fragmentsDevelopment of wound-sealing fibrin bandagesCharacterization of decompression sicknessDevelopment and testing of antiseizure drugsEvaluation of enteric diseases <p>Clinical</p> <ul style="list-style-type: none">Treatment of hypothermiaJaw reconstruction and joint repairSuppression of airway response injuryViral identification and characterizationMetabolic suppression in injury <p>Nonmedical</p> <ul style="list-style-type: none">Evaluating water biomonitoring systems at military sitesDeveloping pollutant toxicity test models <p>Training</p> <ul style="list-style-type: none">Graduate training in surgeryAdvanced life support trainingTraining in humane laboratory animal care and handling <p>Alternatives</p> <ul style="list-style-type: none">Development of noninvasive biosampling techniquesDevelopment of <i>in vitro</i> and theoretical models
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With the end of the Cold War, Congress has mandated that the DoD invest some resources in medical research that directly benefits the civilian population such as research in breast, prostate, and ovarian cancer. These model research programs, developed with guidance from the National Academy of Sciences, account for a considerable portion of DoD extramural animal research and are having an immense impact on the understanding, prevention, and treatment of diverse diseases.

While the underlying requirement for disease research is to protect U.S. military men and women who must operate in a global setting, it should be noted that an indirect benefit of DoD research is its potential application to the broader world community. There the scant resources of many equatorial nations are directed at basic survival needs, such as food and medicine, and not research. There are many examples of the humanitarian benefits of the DoD investment in animal research that are shared on an international basis and improve the quality of life of both humans and animals. Several prime examples of the humanitarian benefits of DoD research efforts are noted in [Table I-2](#).

Table I-2 Humanitarian Benefits of DoD Research Efforts

- The development of transcutaneous immunization by DoD researchers will allow vaccination without skin penetration, a technology of utmost importance for safe immunization in critical settings such as third world regions or refugee camps.
- Malaria is the world's greatest killer and the DoD's fielding of new drugs is critical in the face of the development of resistance to currently fielded drugs. The Army antimalarial researchers have tested over 500,000 drugs for activity against malarial pathogens. One new drug developed by the Army, tafenoquin, is highly effective in both malaria prevention and therapy.
- The DoD collaborated with the Argentine government in the development of a Junin vaccine that has provided critical protection for more than 120,000 individuals in endemic areas of Argentina against the ravages of Argentinian hemorrhagic fever.
- The DoD performs critical diagnostic analyses of suspected disease outbreaks in the United States and overseas and provides vaccine materials for both humans and animals in emergency settings. DoD research facilities were at the forefront of efforts to diagnose and control outbreaks of: (1) deadly hantavirus infection among Navajo Native Americans in 1993; (2) Rift Valley fever in Egypt in 1993; (3) Venezuelan Equine Encephalitis virus in people and horses in central and South America in 1995; (4) Ebola and related viruses in Zaire in 1995; and (5) West Nile virus in New York citizens, horses, and birds in 1999.

Besides the medical benefits of animal research, there are many nonmedical and training benefits. The development of biosensors and the identification of environmental toxins benefit the military and the civilian communities. The DoD has many exceptional medical and scientific educational programs that train both medical personnel and scientists. While these people are in the military, the DoD reaps the benefit of this training; once they leave the military and apply their training in the private sector, this benefit is realized by the civilian community. The development of alternatives to animal use by the DoD provides an extra value to both communities and to animals as they discover ways to reduce or replace the use of animals. Also, refinement research results in more humane methods of performing research that is applied in many types of research settings.

In FY99, the DoD reported over 432 publications in scientific journals, proceedings, technical reports, books, and book sections from RDT&E efforts using animals. Examples of both journal publications and proceedings by research category are presented in [Appendix B](#).

I.3 DoD POLICY GOVERNING ANIMAL RESEARCH

The DoD is committed to full ethical and regulatory compliance for its animal-based research programs. It has been proactive in increasing the fixed infrastructure and span of control necessary to ensure lawful and efficient execution of programs and maximize oversight of diverse and varied missions. The Department has aggressively implemented focused programs and working documents that optimize standardization of animal care and use at the user level. This enhanced standardization and oversight have improved a historically good system, and made it outstanding.

In 1995, the DoD revised and implemented the directive dealing specifically with animal care and use (DoD Directive 3216.1, "The Use of Animals in DoD Programs," 1995) ([Appendix C](#)). This directive strengthens and clarifies requirements for nonaffiliated membership in institutional oversight and directs all DoD animal use facilities that maintain animals for research, testing, and training to attain and maintain AAALAC accreditation. DoD veterinarians, researchers, and policymakers continue in their efforts to be proactive in maintaining the highest level of accountability over animal use.

The DoD also implemented a Policy Memorandum entitled “Department of Defense (DoD) Policy for Compliance with Federal Regulations and DoD Directives for the Care and Use of Laboratory Animals in DoD-Sponsored Programs” ([Appendix D](#)). This 1995 Policy Memorandum specifies training requirements for nonaffiliated DoD Institutional Animal Care and Use Committee (IACUC) members and implements a standard format for animal use protocols ([Appendix E](#)), a standard checklist for IACUC inspections ([Appendix F](#)), and a standard reporting requirement for all animal use research to support a publicly accessible database ([Section II](#)).

All animal research must conform to requirements of the 1966 Animal Welfare Act (Public Law [PL] 89-544) as amended in 1970 (PL 91-579), 1976 (PL 94-279), and 1985 (PL 99-198), as well as the National Research Council *Guide for the Care and Use of Laboratory Animals*, (7th rev. edition, 1996), U.S. Government Principles for Animal Use (1985) ([Appendix G](#)), and the requirements of the applicable regulations of the United States Department of Agriculture (USDA).

Although the Animal Welfare Regulations currently exempt mice and rats in the genera *Mus* and *Rattus* bred for use in research, the DoD has long afforded them, along with all other vertebrates, the same consideration given nonexempt species under the Animal Welfare Regulations. In implementing a full accounting of the use of mice and rats, the DoD is relatively unique in the scientific research community. At the same time, DoD researchers have aggressively developed novel procedures to replace, reduce, and refine the use of animals during experimentation.

I.4 SCOPE OF REPORT

This report provides a comprehensive account of DoD animal care and use programs. There are sections that include in-depth discussions of:

- a. Publicly accessible information on Department research ([Section II](#));
- b. Policies and procedures for oversight of Department animal care and use programs ([Section III](#));
- c. DoD animal use profiles ([Section IV](#)); and
- d. DoD initiatives to promote alternative methods that replace, reduce, or refine animal use ([Section V](#)).

I.4.1 Publicly Accessible Information on Animal Use in the DoD

On October 1, 1995, the DoD implemented a publicly accessible database analogous to the National Institutes of Health Computer Retrieval of Information on Scientific Projects System. The DoD Biomedical Research Database (BRD) is available on-line to the public, and is composed of succinct summaries of Department research projects, allowing interested individuals easy access to Department research information. The cost of animal-based research is presented by work unit summary in the BRD. In order to prevent duplication, this information is not presented in this report. More information on accessing the database is presented in [Section II](#).

I.4.2 Oversight of DoD Animal Care and Use Programs

DoD animal use oversight is reviewed in [Section III](#). In general, internal and external oversight provisions for animal research conducted by the DoD are at least as stringent as those for research in any other department of the federal government, and in many ways exceed the standards. As a matter of policy, the DoD abides by the applicable federal regulations pertaining to animal care and use, including provisions for oversight. All DoD facilities and extramural institutions sponsored by the DoD must submit proposals for animal use to an IACUC. IACUCs review proposed animal protocols to ensure compliance with the Animal Welfare Act (AWA), and address concerns of the community. DoD Directive 3216.1 (1995) establishes oversight requirements that exceed the provisions of the AWA. Each IACUC serves as an independent decision-making body for the institution and establishes policy for the care and use of animals at that facility in accordance with applicable DoD directives, and federal law and regulations.

The DoD has developed and implemented a standardized protocol format for use by all of its units ([Appendix E](#)). It includes requirements for searching the Federal Research in Progress database or an equivalent database and the Defense Technical Information Center database to prevent duplication of ongoing federally funded research. The principal investigator must justify the use of animals, including consideration of alternatives, justify the choice of species and the number of subjects, and include a literature search and assurance that the work does not needlessly duplicate prior experimentation. The protocol must specify procedures to be used with animals and methods to avoid or minimize pain. It must include a literature search for possible alternatives, qualifications of the individuals conducting procedures with animals, and disposition of animals at the termination of the work.

The IACUC ensures that personnel involved in animal-based studies are properly trained and, if necessary, establishes a training program to support the staff. The IACUC inspects facilities and animal care programs at least twice annually, and prepares a written report including a plan to address deficiencies. It enforces compliance with procedures specified in the protocols by conducting inspections, evaluating, and, if necessary, investigating reports of deviation from approved procedures. The IACUC of each facility performs semiannual program reviews of all animal use areas. The DoD 1995 Policy Memorandum ([Appendix D](#)) strengthens that process by establishing a standardized semiannual review checklist that outlines the areas required for IACUC review. This guidance is consistent with the recommendations of the DoD Inspector General (IG) report of February 1994 ([Appendix H](#)). A formal report of inspection shall be prepared twice annually, noting the use of the checklist, and indicating all major and minor deficiencies, a plan for correction of deficiencies, signatures of a majority of IACUC members, and a statement indicating whether there are or are not minority opinions. Finally, the IACUC serves as an impartial investigator of reports of animal care and use concerns and is empowered to suspend the use of animals for protocols not conducted in accordance with the AWA or institutional policy.

DoD Directive 3216.1 (revised in 1995) clarifies composition, membership, and training requirements of the IACUC. The 1995 modification addressed the House Armed Services Committee's request to improve community representation and to appoint animal advocates to the Department's IACUCs, consistent with a recommendation of the IG Report of February 1994. The revised Directive (1995) increased the minimum membership of all DoD IACUCs from three to five. In addition, it specifies that

“there shall be at least one non-scientific member on the IACUC. In addition, there shall be at least one member representing the general community interest who is nonaffiliated with the research facility. The nonaffiliated member and the non-scientific membership can be filled by the same person. To ensure community representation at each meeting and inspection, an alternate to the nonaffiliated member shall be designated for all IACUCs having a single nonaffiliated membership.”

Each DoD IACUC has increased its membership to comply with this Directive. Currently, about 22% of DoD IACUC members are nonscientific.

This Directive exceeds the requirements of the AWA and is further strengthened by the DoD 1995 Policy Memorandum, which requires a minimum of 8 hours of training for new nonaffiliated members. In support of this training, the DoD developed a program consisting of a set of topics and recommended resources that may be used by individual IACUCs.

All animal use programs in the DoD are directed to meet all the requirements for AAALAC accreditation. AAALAC accreditation is recognized as the “Gold Standard” for animal care and use programs. DoD Directive 3216.1 (1995) states that all DoD laboratories that maintain animals for use in research, testing, or training shall apply for AAALAC accreditation. Currently there are 34 DoD animal facilities worldwide. Of these, 100% were accredited in FY99.

During the past 7 years, the DoD has been resolute in pursuing AAALAC accreditation for all of the facilities that use animals in research. This diligence has resulted in an increase in accreditation from 60% in FY93 to 100% in FY99.

DoD oversight responsibility for the Department’s science and technology programs rests with the Director, Defense Research and Engineering (DDR&E). The staff, in conjunction with representatives from the Services, annually review the science and technology efforts to ensure they are fully coordinated and without unnecessary duplication of effort. The preponderance of animal use within the Department occurs in biomedical programs. These activities receive specific oversight from the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee, which was created by congressional direction in 1981. The ASBREM Committee is chaired by the DDR&E and co-chaired by the Assistant Secretary of Defense (Health Affairs). The overall biomedical effort is carefully integrated and reviewed to eliminate unjustified duplication of effort by six subordinate Joint Technology Coordinating Groups reporting to the co-chairpersons.

The DoD has funded the Institute of Laboratory Animal Research (ILAR) of the National Research Council to develop institutional training materials, education, and publications in support of DoD laboratory animal care and use programs since 1987. The Department has resolved to maintain this important collaboration by providing in excess of \$130,000 annually for the ILAR Program.

I.4.3 DoD Animal Use Profiles by Research Category

A profile of DoD animal use is provided in [Section IV](#). In this report, a detailed system was adopted for classifying animal use that includes 8 categories with 23 subcategories: 8 medical research, 4 non-medical research, 3 clinical research, 2 training, and 6 other categories of studies and use. Detailed charts and graphs are included in [Section IV](#).

In FY99, the DoD used 327,097 animals, which is a 12% increase from FY98. Of these, 26,340 (8%) were USDA reportable species as defined in the Animal Welfare Act of 1985. [Table I-3](#) summarizes the major animal use statistics for DoD research.

In addition, it should be noted that no animals were reported as used for development or testing of offensive weapons. During the time that the DoD has been reporting animal use to Congress (FY93-FY99), there has been a 41% decrease in the total number of animals used.

Table I-3 Summary of DoD Animal Use Statistics

Total Animal Use by Species	% of Total
Rodents, fish, amphibians, reptiles, and birds	96.27
Rabbits	1.30
Farm animals (i.e., sheep, pigs, cows, horses, goats, and burros)	1.78
Dogs, cats, nonhuman primates, and marine mammals	0.75
Other	0.09

Percentages may not add up to 100% due to rounding of calculations.

Total Animal Use by Category	% of Use
Medical RDT&E	83.41
Nonmedical RDT&E	5.97
Clinical Investigation	4.40
Adjuncts/Alternatives	3.65
Training & Instructional	1.67
Breeding Stock	0.67
Classified Secret or Above	0.08
Other	0.16

Percentages may not add up to 100% due to rounding of calculations.

I.4.4 DoD Initiatives to Promote Alternative Methods That Replace, Reduce, and Refine the Use of Animals

Congress requested that the DoD establish aggressive programs to replace, reduce, and refine current use of animals. A review of DoD programs and initiatives to develop and implement alternatives to animal research is reviewed in [Section V](#).

Animal research is an essential part of the scientific process, but it is only initiated after due consideration of alternatives. The DoD uses a Standard Protocol Format that specifically requires each investigator to consider alternatives to the use of animals and to justify the animal model selected. The IACUC process includes a strong emphasis on consideration of alternatives in all protocols. All protocols that involve relieved or unrelieved pain or distress require consultation with a veterinarian prior to IACUC review, and a specific database search for scientifically acceptable alternatives to the proposed method. Each protocol that involves animals in research or training must explain the need for the animal research and defend the choice of species as the most scientifically valid model. Often, economies of time and resources are gained when scientifically valid alternatives to animal use are available. Our review of current animal research reveals that scientists in the DoD have developed or adopted many alternative methods based on ethical considerations and other inherent benefits.

General alternatives are those that are frequently implemented in many different DoD programs. Specific alternatives are those that may be specific to both a research protocol and/or facility. Alternatives presented in [Section V](#) are those developed by DoD investigators and the general and specific alternatives implemented by the DoD in FY99. Replacement includes the elimination of animal use altogether, generally by adopting *in vitro* or theoretical model study systems. It also includes the replacement of species that are higher on the phylogenetic scale with those that are lower. Reduction is the use of fewer animals without loss of scientific test validity. Refinements include changes in methods that reduce or eliminate animal distress or pain, or improve animal quality of life.

In FY99, over 600 animal use projects reported that they were implementing alternative methods in animal use. [Table I-4](#) presents examples of alternatives developed by the Department in FY99 to replace, reduce, and refine the use of animals. In addition, the Department sponsors conferences and workshops to promote alternatives to animal research.

Table I-4 Examples of Alternatives for Replacement, Reduction, and Refinement of the Animals Developed or Being Developed by the DoD

- An artificial eye has been developed that mimics the focusing characteristics of the real eye.
- Development of systems to harvest osteoclasts from bone marrow of euthanized swine rather than from live mouse pups.
- Development of a breast tumor cell line that yields innate immune responses to mimic the effects of inflammation on mammary tumor cells *in vitro* and to screen for radiation and drug interactions reduces the number of mice required for research on nonionizing effects of radiation. This technology has a patent issued on it (US Patent #6,013,520, 11 Jan 2000).
- Development of enhanced environmental enrichment by giving ferret colony a larger group holding area with more exploration accommodations.
- A unique housing pyramid was created using Vari-kennels. This enrichment environment offers multiple horizontal surfaces and “caves” that are frequently utilized by our group housed cats.

I.5 CONCLUSION

In conclusion, because the use of animals in research is essential to protect the health and lives of military personnel, the DoD must conduct research involving the use of animals for the foreseeable future. While research has benefited greatly from animal use alternatives, the confounding variables imposed by the complex interactions of organ, tissue, cell, and environmental factors necessitate the continued, judicious use of animal models in DoD programs. Animals are used in research only when scientifically acceptable alternatives are not available. The DoD is committed to full ethical and regulatory compliance for its animal-based research programs, and its animal care and use requirements are as strict or stricter than those required of non-DoD, government-funded, public and private research institutions. DoD policy directs all facilities maintaining animals for use in research, testing, or training to apply for AAALAC accreditation, and the DoD has established programs to replace, reduce, and refine current use of animals.

SECTION II

PUBLICLY ACCESSIBLE INFORMATION ON ANIMAL USE IN THE DoD

II.1 CONGRESSIONAL REQUEST INFORMATION

House Armed Services Committee Report 4301 (1995) requested the Secretary of Defense to “develop a mechanism for providing Congress and interested constituents with timely information... about [Department of Defense (DoD)] animal use programs, projects and activities, both intramural and extramural.” In response to this request, and to serve the interest of both the scientific community and general public, the Department has implemented a publicly accessible database called the Department of Defense Biomedical Research Database (BRD). The BRD is a database containing succinct summaries of the Department’s research projects involving the use of animals. This database is analogous to the National Institutes of Health (NIH) Computer Retrieval of Information on Scientific Projects (CRISP) System. The CRISP System is a biomedical database containing information on research projects supported by the United States Public Health Service, as well as information on intramural research programs of the NIH and the Food and Drug Administration. The BRD became accessible to the public through the Internet on October 1, 1995. It is located on the Manpower and Training Research Information Services home page.

II.2 THE FY98 BRD

The data in the FY98 BRD were developed from the current work unit summary system of the Defense Technical Information Center (DTIC). DoD organizations performing research, development, test, and evaluation (RDT&E) projects are currently mandated to provide annual reports of research to the DTIC. The DTIC maintains these work unit summaries in a database. While the majority of DoD animal use occurs in RDT&E projects, some work is performed in clinical investigations programs that are not mandated to provide work unit summaries to the DTIC. Therefore, the DoD directed that these non-RDT&E DoD animal research projects develop summaries to be entered into the BRD. The areas of research, testing, and training in the FY98 BRD include, but are not limited to, the following: infectious diseases, biological hazards, toxicology, medical chemical defense, medical biological defense, clinical medicine, clinical surgery, physical protection, training, graduate medical education, and instruction.

Military activities that house, care, or use animals provided a work unit summary for any animal-based research. The FY98 BRD contained summaries and was made accessible to the public on October 1, 1999. A work unit summary may refer to a single protocol or a series of protocols that are performed in a given category of animal use. The summaries include the following information:

Title: Title of the work unit.

Funding Fiscal Year: The funding for the entire work for a given fiscal year. The funding includes civilian salaries, cost of animals, cost of materials, cost of human-based research, cost of non-animal-based research, etc. — all costs related to the work unit except military salaries.

POC/Author: The point of contact (POC) for the work unit is usually the Public Affairs Office.

POC Address: The complete mailing address of the POC.

Performing Organization: The name of the activity where the work is performed.

Objective and Approach: This section is a narrative on the objectives and the approach of the work unit. This narrative provides a general summary of the work.

Indexing Terms (Descriptors): A list of indexing terms or keywords. The keywords contain “animals” and the term for any animal types that may be used in the work unit (e.g., guinea pigs, rats).

These summaries were compiled into the BRD and organized into a presentation format for the Internet.

II.3 ACCESS AND USE OF THE BRD

The BRD can be accessed at:

<http://www.dtic.mil/biosys/org/brd/>

The BRD home page shown in [Figure II-1](#) is a searchable database. To perform a search, click on Search. This will bring up the DoD BRD search page. The database can be searched by title, keywords, description, or specific demographic fields ([Figure II-2](#)). The results of the search will produce a hypertext list of titles ([Figure II-3](#)). To access a particular summary, click on the specific title and the summary will appear ([Figure II-4](#)).

II.4 FY99 UPDATE OF THE BRD

The DoD will make all FY99 work unit summaries of animal use in research, testing, education, and training available to the public. The requirement of DoD RDT&E organizations to provide annual reports of research to the DTIC was removed; therefore, the DoD directed that all animal research projects develop summaries to be entered into the BRD. All military activities that house, care, and/or use animals have provided summary information on any animal research, testing, education, or training work for the FY99 BRD via the web-enabled data collection tool. The cost of FY99 animal-based research is presented by work unit summary in the BRD. In order to prevent duplication, this information is not presented in this report. These data will become available to the public on October 1, 2000.

DoD Biomedical Research - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address <http://dticam.dtic.mil/dodbi/index.html> Go

DoD Biomedical Research

Please read this [Disclaimer Notice](#).

Welcome to the DoD Biomedical Research Database. This database has been developed from biomedical research, testing or training programs being federally funded in FY98. The areas of research, testing and training include, but are not limited to, the following: infectious diseases, biological hazards, toxicology, medical chemical defense, medical biological defense, clinical medicine, clinical surgery, physical protection, training, graduate medical education and instruction. This information will be updated on an annual basis at the beginning of the fiscal year.

For further information related to any of the studies included in this database, please contact the point of contact listed with each reference.

[\(FAQ\) Frequently Asked Questions.](#)

Search Tips

The BASIS Web search engine is powerful and simple to use. Most of the searchable fields permit the user to type in any word. The remaining fields provide a pull-down of choices.

Instructions:

- Start a search by typing something in one of the open windows, such as "Keyword".
- BASIS uses Boolean logic to search for data. That means the words "and/or/and not" may be used to limit the scope of a search. The default for this page is "or," meaning the engine will search for any and all combinations of the words provided on the search page. The window that allows the user to select among "and," "or," and "and not" is called "Field Connector" and is located at the bottom right of the search page.
- If you can't remember a name, are not a good speller, or merely want to see what kinds of words are in any of the fields, click on the "Terms" button at the top of the search page. On the next page that appears, select the field you wish to check. Keep in mind, you will get everything in that field, so it might look strange at first.
- If you wish to start over click on the "Search" button at the top of the page, and the search form will again be displayed.

Begin Your Search:

- If you wish to see a listing of all the titles, simply click on "Start Search" without any qualifiers.
- After entering information in the fields that apply to your search, select "Start Search."
- The search results will be displayed on a summary screen listing all references resulting from your search.
- Click on a specific reference to read that specific item.
- Every screen displaying a specific reference has a button marked "Next" at the top of the page. This button can be used to display each succeeding item in the list of references, but you will need to return to the summary screen to view items listed above the specific reference you selected.

[Search FY98 DoD Biomedical database.](#)





For questions and comments:
email@dticam.dtic.mil
 Updated September 30, 1999

Figure II-1 DoD Biomedical Research Database Home Page

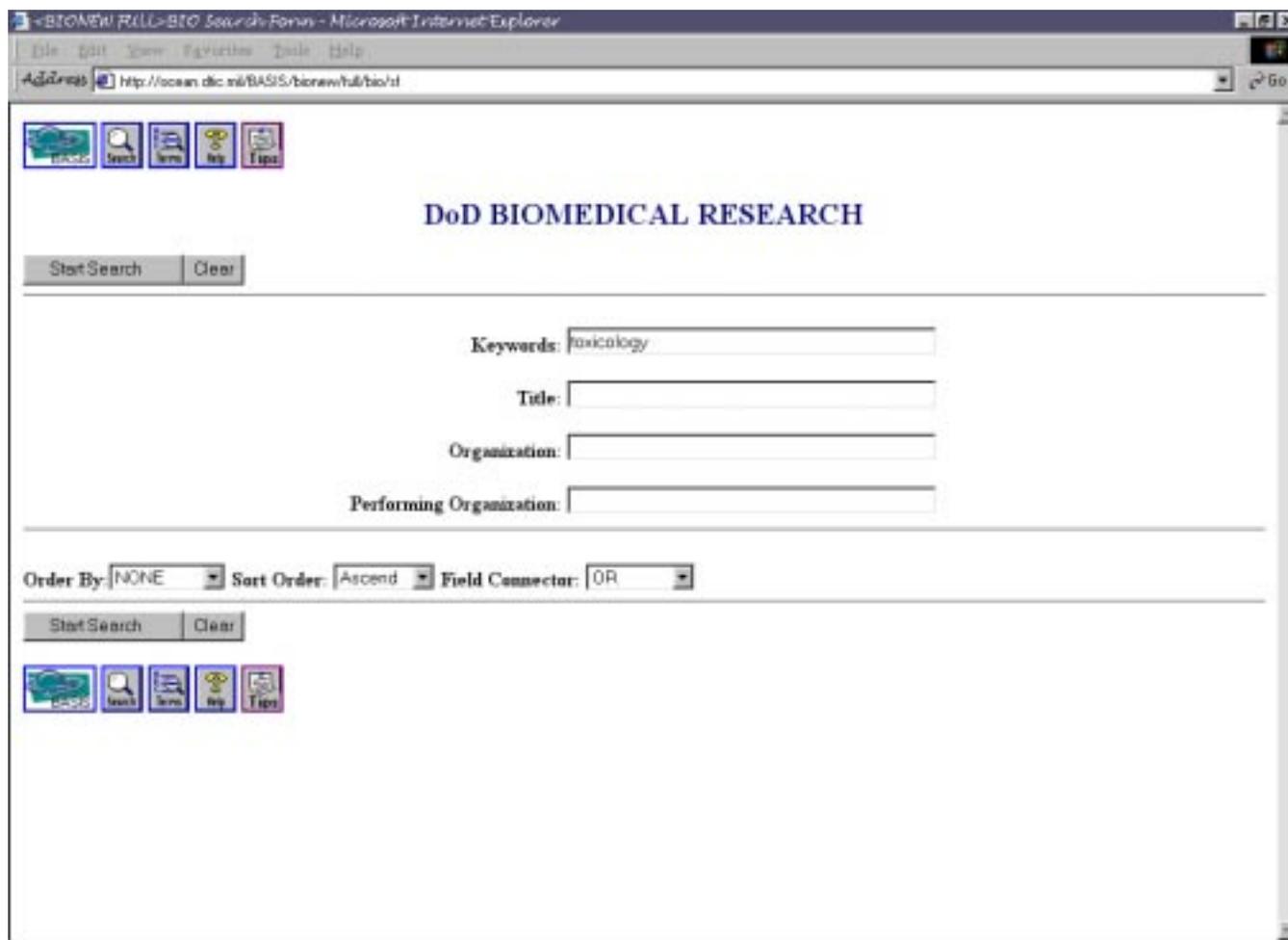


Figure II-2 DoD BRD Search Page

DoD BIOMEDICAL RESEARCH

Documents	Title
1	Quantitative Approaches to Measure and Model Dermal Penetration and Subsequent Chemical Damage
2	Regulation of Metallothionein in Gene Expression
3	Reference Dose Development for JP-4 Jet Fuel
4	An Investigation of the Mechanisms and Pathogenesis of Adult Respiratory Distress Syndrome (ARDS) Related to Smoke Inhalation
5	Biological Effects of Trichloroethylene
6	Predictive Toxicology
7	Health Effects of Imbedded Depleted Uranium
8	Acute Inhalation Toxicity of Chemically Neutralized/Hydrolyzed VX in Rats
9	Perform Preclinical Toxicology Studies of New Drugs

Figure II-3 Search Results on Toxicology from the BRD

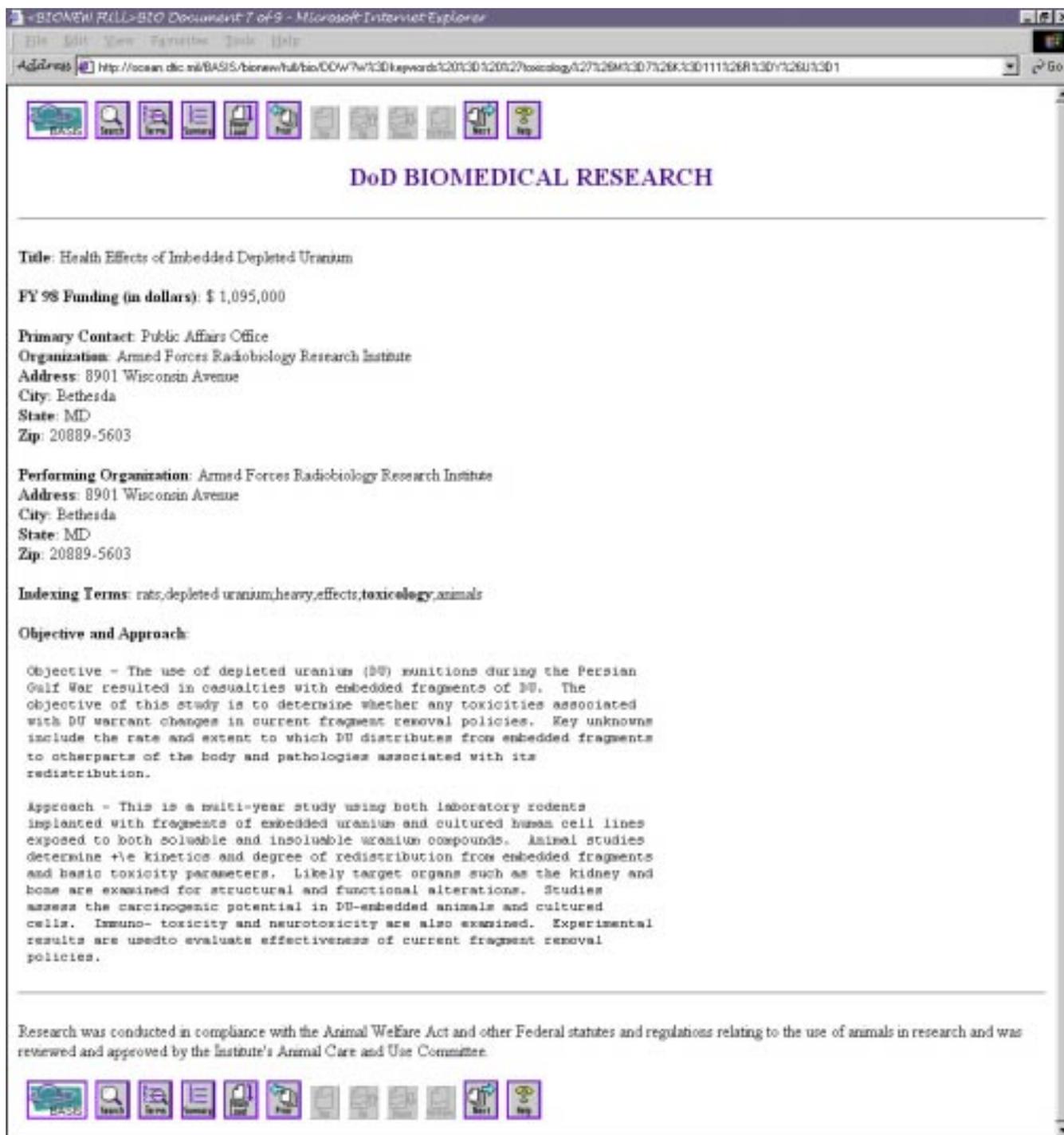


Figure II-4 Sample of Publicly Accessible Summary

SECTION III

OVERSIGHT OF DoD ANIMAL CARE AND USE PROGRAMS

This section of the Department of Defense (DoD) Report to Congress provides a detailed overview of the formal mechanisms and strategies for providing oversight to the Department's numerous animal care and use programs. For the purposes of this report, research is defined as those congressionally authorized science and technology (S&T)-based activities—Title II, Research, Development, Test and Evaluation—of the Military Departments for which funds are appropriated within program elements 6.1 (Basic Research), 6.2 (Exploratory Development), and 6.3 (Advanced Development).

The mechanisms detailed here show a clear and long-standing commitment by the DoD to manage its animal-based research programs in a systematic, comprehensive, and effective manner. Individual programs are driven by specific mission requirements, and are subjected to a thorough, stratified review and analysis prior to commitment of funds. Outside accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) has been mandated to further ensure accountability, the maintenance of high internationally recognized standards, and consistency in the quality of DoD animal use facilities and programs. The DoD uses animals only when necessary to complete its mission, and it does so in full compliance with applicable laws, regulations, and guidelines.

III.1 DETERMINATION OF DoD NEEDS FOR ANIMAL RESEARCH

Determining research needs and plans is a comprehensive process integrated into the DoD's planning, programming, and budgeting mechanisms. Integral elements of these processes are the Department's Research and Development Descriptive Summaries submitted to Congress in justification of the annual budget request. These summaries provide the Office of the Secretary of Defense, the Office of Management and Budget, and Congress with significant detail concerning the accomplishments and future plans of every research project.

Each DoD research laboratory employs its available resources to tailor its organization, staffing, and related infrastructure to best meet its S&T mission and to support the accountability, responsibility, and authority of its commander. In October 1995, the Department implemented a comprehensive DoD Standard Protocol Format (SPF) as a basis to justify and document all proposed animal use ([Appendix E](#)). The SPF solicits specific information that ensures a thorough review of all animal use proposals by Institutional Animal Care and Use Committees (IACUCs). Although there are minor differences in specific procedural elements in protocol review procedures among DoD facilities, DoD regulations ensure that the overall review mechanisms remain fundamentally similar. The general submission, review, and approval processes are summarized here.

An investigator develops a research protocol in support of departmental S&T guidance and other supplementing instructions developed within the chain of command, both external and internal to the laboratory. Augmenting the formal S&T coordination and review process is a literature search to verify nonduplication of previous or ongoing research. The SPF requires that a search of Federal Research in Progress (FEDRIP), or its equivalent, and the Defense Technical Information Center (DTIC) database be made for DoD-funded research. An additional search of the scientific literature in databases such as MEDLINE, GRATEFUL MED, MEDLARS, Animal Welfare Information Center, or Computer Retrieval of Information on Scientific Projects, is highly recommended. Review and certification that this requirement has been met are integral elements of the review and approval process prior to initiation of a research project.

If animal use is planned for the intended research, the principal investigator must prepare an animal protocol request for submission to the facility IACUC. In addition to the DTIC and FEDRIP search, the SPF requires detailed information regarding results and dates of other on-line database searches (e.g., AWIC, AGRICOLA, CAAT, MEDLINE,) that may yield alternatives to painful procedures. Additional pertinent knowledge and information on the proposed study are gained through review of the scientific literature and participation in scientific meetings, symposia, and workshops detailing other ongoing or completed research.

All individual protocols employing DoD resources are reviewed for factors such as military relevance, necessity, scientific merit, and relative research priority. These reviews are normally conducted within the laboratory's command-and-control structure and are characterized by features of peer review systems.

DoD IACUCs carefully review research proposals involving the care and use of animals for numerous factors including, but not limited to, ensuring that: (a) the study is based on sound scientific principles; (b) a minimum number of animals is used to achieve the purpose; (c) the lowest phylogenetic species is selected as the appropriate model; (d) there is appropriate use of analgesics and anesthetics or, if required, there is adequate scientific justification for not using anesthetics and analgesics; (e) the research is not duplicative; (f) the research personnel have the training and experience needed to conduct the research; and (g) the scientific question is of sufficient importance to warrant the use of animals. Additionally, IACUCs are required to address detailed information on research elements such as methodology, techniques, and schedules, greatly facilitating a comprehensive and thorough review by IACUCs.

III.2 OVERSIGHT OF ANIMAL CARE AND USE PROGRAMS AND FACILITIES

There are three principal vehicles for oversight of animal care and use programs at DoD research facilities: Major DoD Activities and Service Command Staff, the local IACUC, and the AAALAC.

III.2.1 Military Departments

Each military department has one or more components responsible for oversight and review of its research facilities and animal care and use programs. Periodic reviews, site visits, and inspections are conducted formally, and reports are prepared as required.

The Army's ultimate oversight responsibility rests with the U.S. Army Medical Command. Within this command, oversight is divided between the U.S. Army Medical Research and Materiel Command and the Army Medical Department Center and School. In both subordinate commands, programmatic guidance and oversight are performed by veterinarians who received specialty training in laboratory animal medicine through the U.S. Army Laboratory Animal Medicine Residency Program.

Ultimate responsibility for laboratory animal care and use in the Navy is divided between the Office of the Chief of Naval Research and the Office of the Surgeon General (OTSG) of the Navy. Oversight for both offices is accomplished by a specialty trained laboratory animal medicine (LAM) veterinarian assigned to the Navy's Bureau of Medicine and Surgery (BUMED). Besides biomedical research oversight for the Navy and the Marine Corps, this LAM veterinarian also serves the Naval School of Health Sciences, Bethesda (Clinical Investigations) and the Inspector General at the Navy's BUMED.

U.S. Air Force responsibility for laboratory animal care and use is provided by the OTSG in addition to the Commanders of the Air Force Research Laboratory, medical centers, and the Air Force Academy. The U.S. Air Force Surgeon's General Research Oversight Committee (SGROC) monitors all animal use protocols, including those performed at Air Force facilities and those contracted to civilian institutions. The SGROC approves all proposed research prior to initiation for projects involving nonhuman primates, companion animals, and marine mammals. A LAM veterinarian is assigned to the Air Force Surgeon's General Office to monitor the animal use research program and serves on the SGROC.

III.2.2 IACUCs

The backbone of the institutional review process for all DoD animal-based research is the IACUC review of the research proposal or protocol. DoD Directive 3216.1, “The Use of Animals in DoD Programs,” ([Appendix C](#)) requires all DoD facilities using animals in research to comply with the Animal Welfare Act (AWA). The AWA requires the Chief Executive Officer to appoint an IACUC, qualified through the experience and expertise of its members, to assess the research institution’s animal program, facilities, and procedures. The AWA requires that IACUCs have a minimum of three members: an appropriately qualified chairman, at least one member not affiliated with the institution in any way other than as a member of the Committee, and a veterinarian with training or experience in laboratory animal medicine and science. Each DoD IACUC is chaired by an individual with credentials and experience appropriate to the post, typically a senior physician, scientist, or veterinarian. DoD Directive 3216.1 clarifies the composition, membership, and training requirements of the IACUC. The 1995 revision to this Directive increased the minimum size of all DoD IACUCs from three to five, which is in concert with the National Institutes of Health (NIH) Office for Protection from Research Risks (OPRR) model. In addition, it specifies that

“...there shall be at least one non-scientific member on the IACUC. In addition, there shall be at least one member representing the general community interest who is nonaffiliated with the research facility. The nonaffiliated member and the non-scientific membership can be filled by the same person. To ensure community representation at each meeting and inspection, an alternate to the nonaffiliated member shall be designated for all IACUCs having a single nonaffiliated membership.”

In FY99, the 35 IACUC panels reporting animal use averaged 9 members each, a slight increase from that of FY98. Private civilian, government civilian, and military representation on the panels was 7%, 39%, and 54%, respectively.

The diverse backgrounds/professions of the voting (non-alternate) IACUC members are provided in [Figure III-1](#). Occupations/vocations for the alternate IACUC members are presented in [Appendix I](#). Currently, 19% of the voting members are not affiliated with the institutions of their IACUCs. Of these 6% are private sector civilians; the remainder are federal government civilians or military personnel. In accordance with DoD Directive 3216.1, these members represent the community and are not affiliated with (not under the command of) the research facility.

This Directive exceeds the requirements of the AWA and is further strengthened by the DoD 1995 Policy Memorandum ([Appendix D](#)) that directs a minimum of 8 hours of training for the new nonaffiliated members. DoD IACUCs implemented these requirements October 1, 1995. All DoD new nonaffiliated IACUC members received at least 8 hours of training to fulfill the requirement. An average of 13.8 total hours of training was reported for nonaffiliated IACUC panel members in FY99.

Each IACUC has at least one Doctor of Veterinary Medicine with training or experience in laboratory animal science and medicine who serves as an animal advocate. The U.S. Army Veterinary Corps’ formal postgraduate training program in laboratory animal medicine provides

IACUC Membership by Occupation 307 Voting IACUC Members	
Professions	%
Research Scientists	25%
Veterinarians	24%
Other Nonscientists*	22%
Physicians	14%
Animal Technicians	5%
Statisticians	3%
Other Medical**	4%
Clergy/Ethicists	3%

* Other nonscientist occupations are listed in [Appendix I](#).

**Nurses, Dentists, Lab Technicians, Pharmacists

Percentages may not add up to 100% due to rounding of calculations.

Figure III-1 Background Professions of IACUC Members

didactic training in IACUC composition, function, and regulatory requirements. This training also prepares them to serve as animal advocates. The 35 DoD institutions reporting in FY99 reported an average of 2 veterinarians serving on their IACUC panels; 19 IACUC panels had 2 or more veterinarians.

It is a proactive Department policy that nonaffiliated members participate fully in discussions and vote on all research proposals. They are also encouraged to perform unannounced site visits of animal care facilities. In FY99, nonaffiliated members made 25 unannounced visits to Department animal facilities.

The IACUC has statutory responsibility for reviewing the facility's animal care and use program and inspecting the animal facilities on a semiannual basis. Consequently, at least once every 6 months, each IACUC performs an in-depth review of the animal care and use program and inspects the animal facilities. To facilitate these inspections, the DoD has developed and implemented a standardized semiannual program review checklist that details the requirements of the review. All DoD IACUCs use a standardized checklist for their semiannual program reviews. The IACUCs prepare written reports of their evaluations and submit them to the Institutional Official, usually the facility commander. Reports specifically address compliance with the AWA, identify any departures from the Act, and include an explanation for the departure. The report must distinguish between major and minor deficiencies and provide a schedule for the resolution of deficiencies.

All DoD IACUCs document their meetings and activities, including the results of inspections, complaints, actions, and training. They are empowered to review and investigate concerns involving the care and use of animals at the research facility resulting from complaints received from the public, in-house workers, or reports of noncompliance received from laboratory personnel. To facilitate the reporting and resolution of complaints or concerns, facilities commonly place signs or notices in high-traffic areas and in animal study areas advising both the public and personnel who work with animals how to contact members of the IACUC, facility commanders, and/or the Inspector General (IG) whenever questions arise concerning humane care and treatment of animals. Among the reporting DoD institutions, only one complaint was registered during FY99. DoD facilities have developed a wide variety of proactive and innovative mechanisms to inform the public how to contact responsible individuals and to ensure that those who work with animals are fully apprised of the requirement to provide humane and ethical care ([Appendix J](#)). Additionally, IACUCs make recommendations to the Institutional Official regarding any aspect of the research facility, its animal program, or the training of its personnel. They review and approve, require modification to, or withhold approval of research protocols involving the use of animals, and suspend an activity involving animals when they determine that the activity is not being conducted in accordance with its approved protocol.

III.2.3 AAALAC

The AAALAC is a nonprofit organization chartered to promote high quality standards of animal care, use, and welfare through the accreditation process. The AAALAC accreditation process provides scientists and administrators with an independent, rigorous assessment of an organization's animal care and use program.

The DoD recognizes the benefits of accreditation by the AAALAC and is committed to continuing its full participation in the AAALAC accreditation process in order to effect external peer review for assessing program compliance with regulations, guidance, and ethical responsibility. With the publication of the Joint Regulation on the Use of Animals in DoD Programs, June 1, 1984 (AR 70-18), the DoD implemented more stringent animal care and use requirements than those required by statute. The Joint Regulation established uniform procedures, policies, and responsibilities for the use of animals in the DoD. The DoD has elevated the requirement with the current DoD Directive 3216.1 (1995), which states that "all DoD laboratories that maintain animals for use in research, testing, or training shall apply for AAALAC accreditation." To increase accountability and tracking, a centralized DoD point of contact and database for AAALAC information has been established to enhance monitoring, reporting, and facilitation of the AAALAC accreditation process.

The Joint Service Regulation also cites the National Research Council (NRC) publication, *Guide for the Care and Use of Laboratory Animals*, which is the principal document used by AAALAC in its accreditation process. The animal care and husbandry standards and requirements contained in the Guide are designed to provide an environment that ensures proper care and humane treatment are given to all animals used in research, testing, and training. This care requires scientific and professional judgment based on knowledge of the husbandry needs of each species, as well as the special requirements of the research program.

III.2.3.1 AAALAC Accreditation

AAALAC accreditation is widely accepted by the scientific community, and viewed as an extremely desirable feature of the Department's animal care and use programs. The Association is highly respected as an independent organization that evaluates the quality of laboratory animal care and use both in the United States and overseas. Accreditation covers all aspects of animal care including: institutional policies; laboratory animal husbandry; veterinary care; facility physical plant; support facilities; and special areas of breeding colony operations and animal research involving hazardous agents such as radioactive substances, infectious agents, or toxic chemicals.

The independent and external peer review that is fundamental to continuing AAALAC accreditation is valuable to any program. Regular, periodic AAALAC inspections highlight program strengths and identify potential weaknesses, and laboratories maintaining accreditation demonstrate a high degree of accountability and program excellence. AAALAC standards also stress the appropriate appointment, composition, and empowerment of IACUCs.

III.2.3.2 AAALAC Accreditation Status for DoD Programs

The number of DoD AAALAC institutions that maintain animals for research, testing, and/or training has significantly increased over the past 7 years (Figure III-2). Worldwide, all 34 DoD institutions with animal holding facilities reporting animal use in FY99 are AAALAC accredited. Of the three institutions not accredited in FY98, one has since eliminated animal use, one received accreditation, and the third is not eligible for AAALAC accreditation as it employs only transient animal use and does not have an animal use facility [U.S. Army Landstuhl Regional Medical Center (LRMC) in Germany]. Four small detachments assigned to DoD bases share animal use facilities but maintain their own animal care and use programs. Appendix K provides additional information on AAALAC accreditation by program.

There are four DoD research laboratories and one medical center using animals outside the United States. In foreign countries, issues of sovereignty often complicate the accreditation process; local governments

that must be considered. Renegotiation of various agreements may be involved in construction or renovation projects. Despite these and various other impediments, the DoD has raised the standard of excellence in its animal care and use programs and facilities by receiving full accreditation for all four of its overseas research laboratories. The Navel Medical Research Detachment in Lima, Peru, the Naval Medical Research Unit #2 in Jakarta, Indonesia, and the

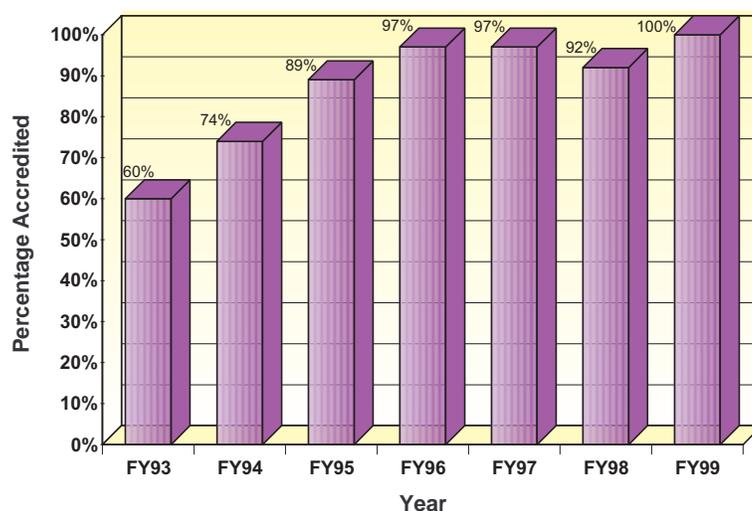


Figure III-2 DoD AAALAC Accreditation FY93 to FY99

Naval Medical Research Unit #3 in Cairo, Egypt were the first laboratories to be AAALAC accredited in South America, Southeast Asia, and Africa, respectively. The animal facility of the Armed Forces Research Institute of Medical Sciences in Bangkok, Thailand recently completed a 50-million dollar renovation and was accredited in 1999. The LRMC has an animal use program with IACUC and veterinary oversight and uses a small number of animals for medical training four times a year. Since LRMC does not have an animal holding facility, animals are housed in temporary facilities for less than 24 hours and AAALAC accreditation is not possible.

III.2.4 DoD Program Reviews

The DoD utilizes external peer review by the Joint Commission for Accreditation of Health Organizations to evaluate many of its programs such as drug screening laboratories and military medical facilities. At the same time, the DoD recognizes the diversity of mission operations and the global reach of the military mission. There are situations where external peer reviews are not cost effective due to remote locale, limited scope of operations, or host nation sovereignty. In these cases, equivalency standards can be applied and effectively monitored. The Joint Service Regulation and Service-conducted inspections of facilities implement the requirements of the AWA and the 1996 NRC *Guide for the Care and Use of Laboratory Animals*.

III.2.5 Training

The DoD provides extensive veterinary and animal care services for its facilities. Veterinarians with specialty training in LAM direct programs for animal care and use throughout the Department. They serve as a valuable resource to the research staff and the IACUC to ensure that all research methods and maintenance procedures are consistent with the latest principles of animal medicine, and with the current interpretations and implementing regulations of the AWA. The DoD sponsors formal postdoctoral training programs for veterinarians in LAM, including a nationally recognized, in-house 4-year program consisting of 2 years of residency training and 2 years of practical experience, culminating in specialty board eligibility for certification by the American College of Laboratory Animal Medicine. In August 1995, the DoD began a formal postgraduate Master's of Public Health in Laboratory Animal Medicine at the Uniformed Services University of the Health Sciences (USUHS). This outstanding program provides the Department with a new source of LAM experts who will significantly enhance animal welfare in our research laboratories. Many DoD veterinarians attend the USUHS postgraduate LAM training program resulting in a master's degree in public health. It is significant that approximately 28% of the current membership of American College of Laboratory Animal Medicine, the veterinary specialty most closely associated with animal welfare and laboratory animal care and use, received either all or part of their training in DoD-sponsored LAM training programs.

In addition to veterinarians, the DoD trains animal care specialists (Military Occupation Specialty 91T) to assist in the daily management, care, and treatment of laboratory animals. Over the last 31 years, the DoD has trained over 4,300 animal care specialists. Since 1986, the Division of Veterinary Medicine Walter Reed Army Institute of Research (WRAIR) has continued to sponsor the DoD Laboratory Animal Workshop program. Some workshops taught there focus on species-specific techniques and handling, while others provide general laboratory animal information required by federal law and other guidelines for the research mission. Successful completion of the workshops fulfills the training requirements for use of those animals in research protocols. The DoD Laboratory Animal Workshops at the WRAIR trained over 300 investigators (16%) and technicians (84%) in FY99, and the course schedule is provided in [Appendix L](#). Additionally, DoD research institutions send appropriate staff to a variety of seminars and workshops sponsored by the NIH, other federal agencies, and private institutions dedicated to the proper care and use of research animals. The Annual Public Responsibility in Medicine and Research Meeting is an outstanding example of this type of training.

The DoD provides detailed informational and instructional material to all members of the IACUC, including nonaffiliated members, to ensure that they are fully cognizant of the numerous

responsibilities of IACUC members under the provisions of the AWA. DoD Directive 3216.1 “The Use of Animals in DoD Programs” requires new nonaffiliated IACUC members to receive an initial 8 hours of training and continued training for IACUC members, investigators, and technicians. This requirement went into effect October 1, 1995. Although training is an individual institute’s responsibility, the DoD has developed a program consisting of a set of topics and recommended resources to support the training requirement ([Appendix M](#)). The topics are meant to be general and allow for tailoring of the training to meet an institute’s specific needs. The recommended resources are readily available. Formal training on animal care and use issues is provided to all appropriate personnel in Department research laboratories in accordance with the provisions of the AWA. Examples of training or materials currently provided to IACUC members are detailed in [Appendix M](#). One of the examples listed in [Appendix M](#) is the Institute of Laboratory Animal Research publication, *Education and Training in the Care and Use of Laboratory Animals*. As one of the major sponsors of this publication, the DoD has established a formal relationship with the NRC, an extension of the National Academy of Sciences. The publication is used as a guide by the DoD and has been translated into five languages. Many countries use this publication as a standard for the care and use of laboratory animals.

III.2.6 Community Visits

Individuals or groups wishing to visit Department facilities need to comply with certain procedural guidelines. All DoD facilities are served by a public affairs office, at either the facility, post, or base. Visits by the public or the press are arranged and coordinated through the appropriate public affairs office. While most facilities reported few community visits, 212 community visits were described in FY99, a 4.4-fold increase over that in FY98. DoD facilities are visited by various special interest groups including community and civic groups; animal welfare or animal advocates, groups, or individuals; dignitaries, academia, and teachers; local, state, and national politicians; congressional members and staff; and elementary to postdoctoral students. Consequently, a greatly diversified range of individuals is constantly visiting and observing the quality of Department facilities.

III.2.7 Office for Protection from Research Risk Oversight

A number of DoD research laboratories participate in the NIH grants process. Institutional compliance with the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS Policy) is a prerequisite for granting or continuation of NIH intramural and extramural funding. The formal vehicle for compliance with the PHS Policy is an “Animal Welfare Assurance” negotiated between individual institutions and the OPRR. The principal references for the negotiation of an OPRR “assurance” are the Health Research Extension Act of 1985 (Public Law 99-158, November 20, 1985, “Animals in Research”), the AWA, and NRC’s *Guide for the Care and Use of Laboratory Animals*. Consequently, OPRR provides additional oversight to those laboratories that have negotiated OPRR assurances.

III.2.8 Additional Oversight

Within the DoD, individuals may raise animal welfare concerns. This may be with the IACUC, facility commanders, the IG, or the attending veterinarian. Other means of noncompliance or concern may be voiced through “Waste, Fraud and Abuse Hotlines,” or the formal chain of command. Procedures to enhance and facilitate these mechanisms have been implemented in DoD facilities.

The function of the IACUC and the role of an ombudsman are augmented by the Department’s IG. An ombudsman is defined in Webster’s dictionary as “a government official charged with investigating citizens’ complaints against the government.” The Humane Society of the United States, a witness at the April 7, 1992 hearing on The Use of Animals in Research by the Department of Defense before the House Armed Services Committee, offered the Ombudsman Program at the Massachusetts Institute of Technology as an example of a model program. This program consists of an ombudsman assigned to the university president’s office to hear complaints regardless of the nature. These include personnel complaints, sexual harassment, animal welfare, etc. The DoD assigns this responsibility to its IG and IGs of the Military

Departments. In addition, military bases and large organizations on military bases have their own IGs who fulfill this function. Significantly, complaints to an IG can be made anonymously. Also of note is the fact that IG investigations are conducted with complete autonomy, and are completely insulated and immune to pressure from the chain of command.

Oversight of extramural (contract) animal-based research is provided for in DoD Directive 3216.1 (1995) ([Appendix C](#)). It states that

- a. “all extramural research proposals using live animals shall be administratively reviewed by a DoD veterinarian trained or experienced in laboratory animal science and medicine before grant or contract award.
- b. “the most recent [U.S. Department of Agriculture] USDA inspection reports are provided or obtained for the facility under consideration for a research contract or grant using animals, and that during the term of the award, the most recent USDA inspection reports be reviewed on an annual basis.
- c. “a DoD veterinarian trained or experienced in laboratory animal science and medicine shall conduct an initial site visit to evaluate animal care and use programs at contracted facilities conducting DoD-sponsored research using nonhuman primates, marine mammals, dogs, cats, or proposals deemed to warrant review. The initial site visit shall occur within 6 months of when the facility has taken delivery of the animals under DoD contract or grant award. Any facility receiving a DoD-funded grant or contract for animal-based research shall notify the DoD component sponsor and shall have a site inspection within 30 days of notification of loss of AAALAC accreditation for cause, or notification that the facility is under USDA investigation. Site inspections for cause shall evaluate and ensure the adequacy of animal care and use in DoD-sponsored programs, and provide recommendations to the sponsoring DoD component about continued funding support of the research.”

As directed by DoD Directive 3216.1, all nonhuman primate protocols receive an additional centralized review external to the research facility.

III.3 CHAIN OF COMMAND OVER ANIMAL CARE AND USE PROGRAMS

The chain of command is designed to resolve problems at the lowest possible level. It provides control and communication among various components of organizations. Each link in the chain of command is a level of responsibility and authority that extends from the President of the United States, as Commander in Chief, down to the lowest supervisory level. Different levels within the chain have different responsibilities and authority. Each level in the chain is responsible for a lower level and accountable to a higher one. Every individual in the military is part of the chain of command and is accountable to it.

III.4 AVOIDANCE OF UNINTENDED DUPLICATION OF RESEARCH

Both the DoD and Congress have a long history of concern about the potential for unintended duplication of Defense research. Within the past decade, the Department has initiated significant improvements in its mechanisms for coordination, and joint planning and review of its research programs.

In 1981, Congress expressed concerns about the potential for unnecessary duplication of biomedical research among the Military Departments (H.R. 96-1317). This resulted in the DoD proposing an Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee to coordinate biomedical research planning and the conduct of biomedical research among the Military Departments. Congress fully endorsed and built upon this proposal by establishing DoD Lead Agencies for major elements of the biomedical research programs for which there were either no, or very few, service-unique requirements (H.R. 97-332). For example, the Army was designated the DoD Lead Agency for military infectious disease and combat maxillofacial research while the Navy was designated DoD Lead Agency for preventive and

emergency dentistry research. The ASBREM Committee established Joint Technology Coordinating Groups (JTCGs) (Figure III-3), consisting of directors of biomedical research programs and representatives of biomedical research laboratories, to coordinate all DoD biomedical research planning and execution. The ASBREM Committee process has proven to be highly effective at eliminating unnecessary duplication of biomedical research.

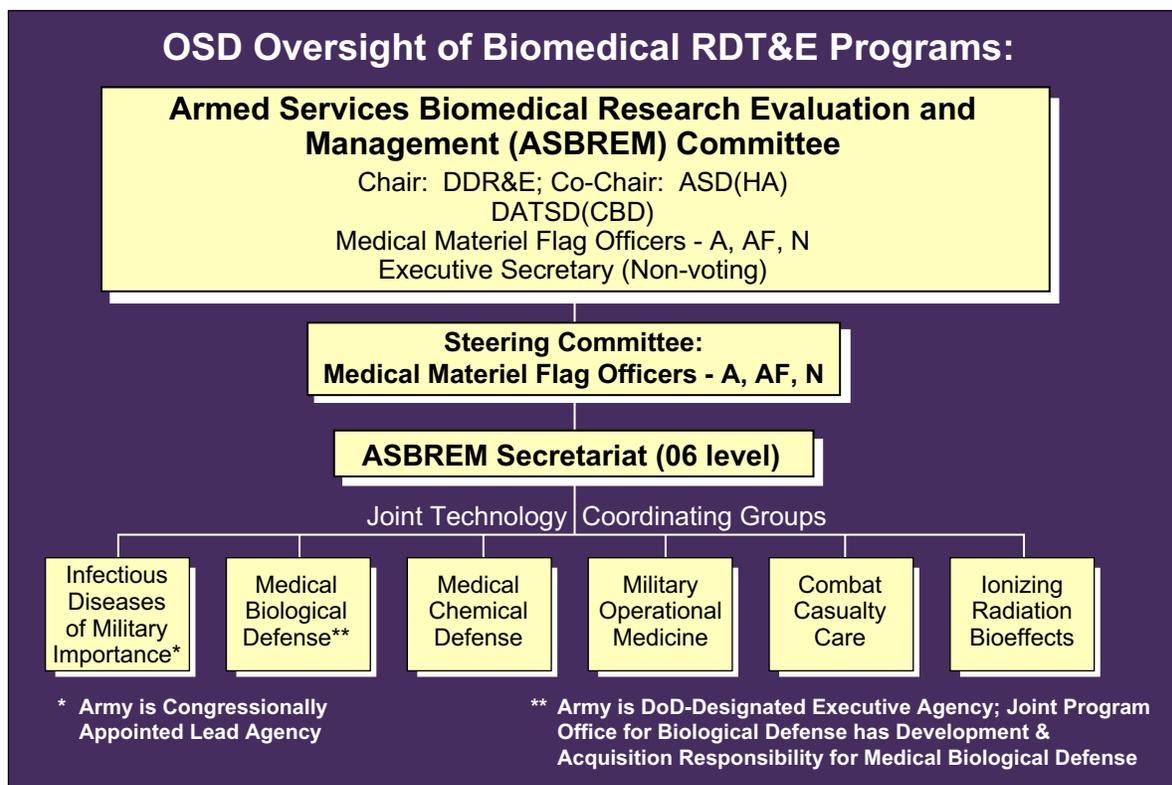


Figure III-3 Structure of ASBREM Committee

Because of the wide range of organizations and variations in process between the Military Departments and Defense Components, the DoD uses a variety of mechanisms to coordinate its research and training. The ASBREM Committee process became the model for joint DoD coordination initiatives. Responsibility for joint coordination, planning, execution, and review of the Department's S&T programs was assigned to joint oversight bodies: the Joint Directors of Laboratories (JDL), the ASBREM Committee, the Training and Personnel Systems Science and Technology Evaluation and Management (TAPSTEM) Committee, and the Joint Engineers. The resulting technology area responsibilities are shown in Figure III-4. TAPSTEM oversees DoD personnel and training research (Figure III-5) and the Joint Engineers oversee environmental quality and civil engineering (Figure III-6). The JDL is responsible for general oversight as well as specific joint planning for Combat Materiel (Figure III-7). These oversight bodies are assisted in execution of their responsibilities by subordinate S&T coordinating groups that are focused on coordination of specific technology areas. For example, the ASBREM and TAPSTEM Committees are supported by the JTCGs, (Figures III-3 & 5) and Joint Engineers and the JDL are supported by separate technology panels (Figures III-6 & 7). Under this process, researchers and managers from the service laboratories jointly plan execution and coordinate their research to minimize redundancy and take advantage of each other's strengths.

One of the primary ways that the DoD prevents unnecessary duplication is by the use of the DoD SPF (Appendix E). The DoD policy for compliance with federal regulations and DoD Directive for the care and use of laboratory animals in DoD-sponsored programs (Appendix D) requires that all intramural protocols involving animals use the SPF. It also requires that all extramural contractors provide all of the pertinent information contained in the SPF. The SPF requires that the principal investigator perform a literature search of Federal Research in Progress and Defense Technical Information Center databases on their equivalent to prevent unnecessary duplication of effort. The principal investigator signs an assurance statement to document that the search was performed.

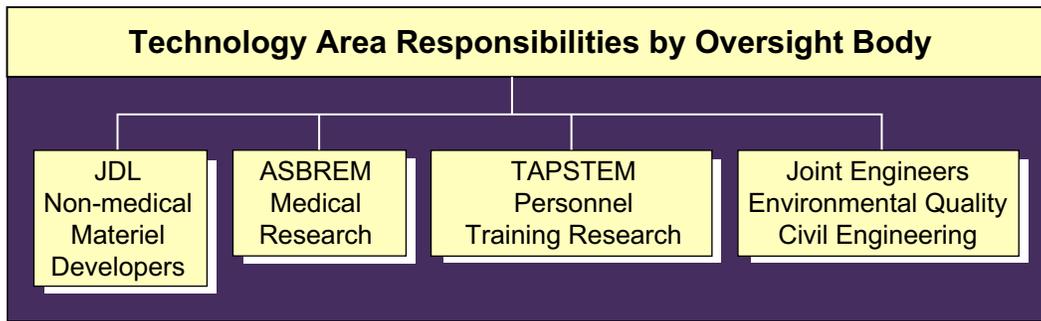


Figure III-4 DoD Technology Area Responsibilities

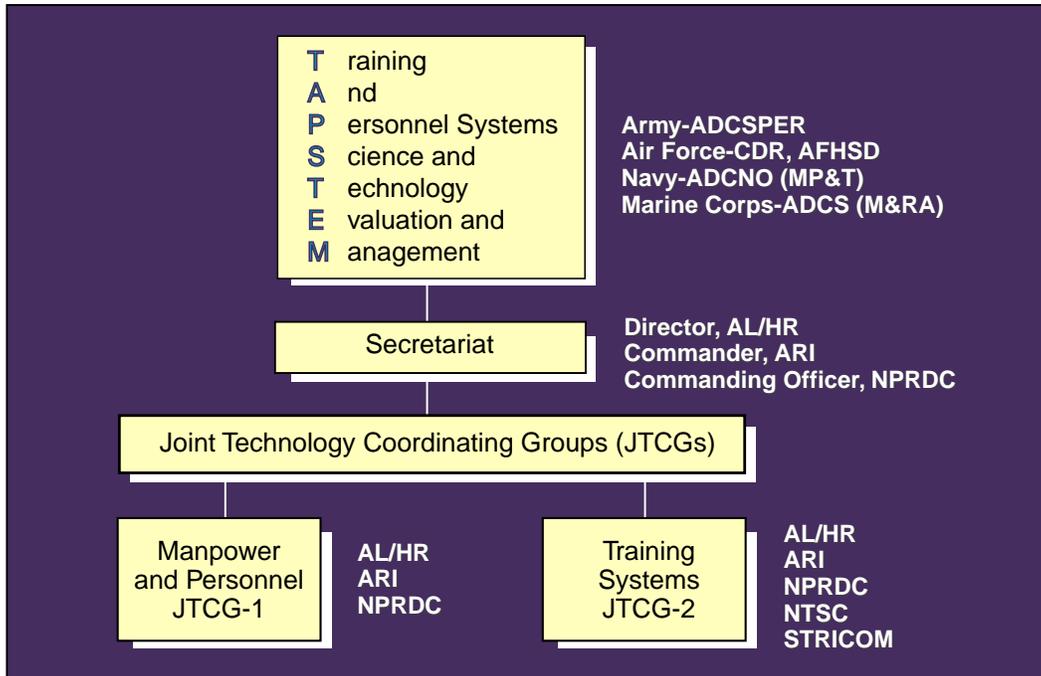


Figure III-5 TAPSTEM Organization

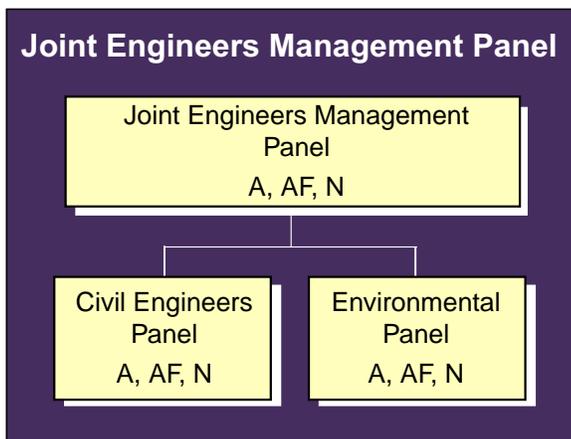


Figure III-6 Joint Engineers Management Panel



Figure III-7 JDL Technology Panels

In addition to these formal coordination and review processes to eliminate research duplication, there are a number of less formal mechanisms that provide significant disincentives for research duplication. Competition, both in-house and extramural, for research support is a prominent feature of S&T; each year large numbers of scientifically meritorious research proposals cannot be funded due to shrinking resources and funding shortages. In most cases, the professional stature of individual scientists or engineers among their peers is measured by their individual and original contributions to the scientific literature. There is little if any reward for unnecessarily duplicating the work of others; such actions often have significant negative impact on how the scientist or engineer is viewed by peers and on the ability to secure research support. Additionally, within the DoD civilian personnel system, scientists' and engineers' pay grades are determined in part by the level of individual scientific and technological contributions. One outcome of research is publication of a manuscript in a professional journal. A sample listing of journals with DoD animal research publications is found in [Appendix B](#). Peer-reviewed journals critique the research during the review process, leading to an overall enhancement of the research process and to validation of both the scientific merit and necessity of the research. These less formal, relatively unquantifiable, disincentives substantially augment and buttress the Department's formal mechanisms for regulating and avoiding unnecessary research duplication within its S&T programs.

III.5 AVOIDANCE OF UNNECESSARY RESEARCH

The same factors that effectively prevent unwarranted duplication of research are applied to prevent unnecessary research. Additionally, through Cooperative Research and Development Agreements, the Department has increased its emphasis on leveraging and exploiting, for Defense needs, S&T investments from other federal agencies, U.S. industry, and academic institutions, and the international scientific community. Past descriptions of Defense S&T "spin-off" have been supplanted by programs intended to "spin-on" accomplishments by others as well as to optimize the dual-use potential of the Defense S&T investment. The foundation of Defense S&T strategy is the application of S&T accomplishments to sustain Defense technological superiority through efficient and responsive modernization of our warfighting capabilities.

III.6 SUMMARY

Research using animals is highly structured and regulated in the United States, being governed by numerous laws, regulations, and policies. Consequently, the DoD has a number of stratified formal and informal mechanisms for reviewing, regulating, and executing its animal care and use programs. Research performed by the DoD receives close programmatic, scientific, and regulatory scrutiny, being carefully reviewed by various offices, committees, and program managers before it is funded or implemented. These reviews serve to determine the necessity to the mission, provide oversight of animal care and use, and avoid unnecessary or unintended duplication of research.

Individual IACUCs provide oversight of animal care and use programs and research. They also provide training and information about animal care and use, and ensure the humane use of animals in research. Each DoD facility's IG is also an effective means for investigation of concerns about the necessity of animal use, as well as the ethical treatment and humane care of animals used in DoD research.

DoD policy dictates that all institutions that maintain animal facilities must seek AAALAC accreditation. AAALAC accreditation ensures that DoD laboratories will receive independent evaluation and maintain similar high standards.

Over the past decade, the DoD, in concert with Congress, has streamlined and greatly improved coordination of its S&T activities to avoid unnecessary duplication and provide a focused program of research responsive to the DoD's unique and wide-ranging needs.

When viewed in its totality, the Department's significant progress and investment in administration, infrastructure, standardization, training, and oversight of animal use are indeed impressive, and can serve as useful models for the rest of the animal use research community.

SECTION IV

DoD ANIMAL USE PROFILES

The information presented in this section provides profiles on the reported use of animals in various research categories, and the U.S. Department of Agriculture (USDA) pain categories of Department of Defense (DoD) animal-based research, testing, and training programs for fiscal year (FY) 1999.

IV.1 METHODS

Information was solicited and received from DoD agencies and military commands, organizations, and activities involved in animal care and use programs located both inside and outside of the United States. These included extramural contractors and grantees that performed animal-based research. For the purpose of this reporting requirement, an intramural program represents research performed at a DoD facility and funded by either DoD or non-DoD funds. An extramural program represents research performed by a contractor or grantee that is funded by the DoD.

IV.1.1 Animal Use Profiles

The animal use profiles prepared for this report are consistent with the reporting information and data provided to the USDA Animal and Plant Health Inspection Service (APHIS) Form 7023. In addition, this report contains comprehensive information on all other animals (e.g., mice, rats, birds) used that are not required in reports to the USDA.

For the purposes of this reporting requirement, an animal was defined as any whole nonhuman vertebrate, living or dead, excluding embryos, that was used for research, development, test, and evaluation (RDT&E), clinical investigations, diagnostic procedures, and/or instructional programs. Only live animals or whole dead animals, as defined, that were either on hand in the facility or acquired during FY99 and used are included. Animal organs, tissues, cells, blood, fluid components, and/or byproducts purchased or acquired as such animal/biological components are not reported. This definition does not include animals used or intended for use as food for consumption by humans or animals, animals used for ceremonial purposes, or military working animals and their training programs.

A single animal was counted only once in determining the number of animals used during the fiscal year for a particular work unit or protocol. This does not refer to the number of times an individual animal was injected, manipulated, handled, or administered medication and/or experimental compounds within a given work unit, protocol, or program. Animals on hand during FY99 but not actually used during the fiscal year are not included in this number.

IV.1.2 Animal Use Categories

All DoD agencies and military commands, organizations, and activities involved in the performance and/or funding of animal care and use programs reported animal work by the category that best describes the general research purpose of the animal use. The 8 general categories and 23 specific subcategories are listed in [Table IV-1](#). If the research categories provided did not adequately describe the animal use within each particular work effort, the animal was placed in the Other category. In-depth information on specific activities performed within a subcategory is presented in [Appendix N](#). The medical research categories correspond to the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee's Joint Technology Coordinating Group Medical Research Areas. Nonmedical categories consist

Table IV-1 Animal Use Categories

<p>MEDICAL (M) M1: Military Dentistry M2: Infectious Diseases M3: Medical Chemical Defense M4: Medical Biological Defense M5: Human Systems Technology M6: Combat Casualty Care M7: Ionizing Radiation M8: Other Medical RDT&E</p> <p>NON-MEDICAL (N) N1: Physical Protection N2: Physical Detection N3: Offensive Weapons Testing N4: Other Non-Medical RDT&E</p> <p>CLINICAL INVESTIGATIONS (C) C1: Clinical Medicine C2: Clinical Surgery C3: Other Clinical Investigations</p>	<p>TRAINING/INSTRUCTIONAL (T) T1: Training, Education, and/or Instruction of Personnel T2: Other Training/Instruction</p> <p>ADJUNCTS/ALTERNATIVES TO ANIMAL STUDIES (A) A1: Adjuncts to Animal Use Research A2: Alternatives to Animal Investigation A3: Other Alternatives/Adjuncts</p> <p>CLASSIFIED SECRET OR ABOVE STUDIES (S): Classified secret or above studies on animals</p> <p>ANIMAL BREEDING STOCK (B): Animals maintained for breeding</p> <p>OTHER ANIMAL USE CATEGORIES (O): Other animal use purposes</p>
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of RDT&E programs performed outside the ASBREM Committee medical oversight. Clinical Investigations studies were performed under the auspices of the Assistant Secretary of Defense for Health Affairs and the military services medical departments through Major Force Program 8 funding. These studies were usually in support of graduate medical education training programs located at the major military medical centers.

IV.1.3 USDA Pain Categories

The USDA requires that all institutions using any regulated animal for research, testing, training, or experimentation register with the USDA as a research facility and submit an annual report. This annual report presents the number of regulated animals used and the type of pain or distress, if any, to which the animals were exposed.

The USDA has developed three pain categories for its reporting requirement (Table IV-2). All animals herein reported are assigned to one of the three USDA pain categories; this includes animals that are not regulated by the USDA. The USDA requires that any reporting facility that uses procedures producing unalleviated pain or distress file an explanation of the procedures with its annual APHIS report.

Table IV-2 USDA Pain Categories
(USDA APHIS Form 7023)

<p>USDA COLUMN C Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.</p> <p>USDA COLUMN D Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.</p> <p>USDA COLUMN E Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests.</p>

The animals reported in Column C of the USDA report are those used in a procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure was applied. Procedures performed on these animals are those that are usually conducted on humans without anesthesia or analgesia. Examples include most blood-sampling techniques (excluding intracardiac blood sampling), injections, and tattooing.

The animals reported in Column D of the USDA report are those in which pain is alleviated by appropriate anesthetic, analgesic, or tranquilizing drugs. Examples include anesthesia for surgical procedures or catheter placement, and analgesia during recovery from surgery.

The animals reported in Column E of the USDA report are those that would experience more than slight or momentary pain or distress that cannot be alleviated by drugs. Examples of procedures where drugs were not used because they would have adversely affected the procedures, results, or interpretation of the research, or tests include some infectious disease studies and some toxicology studies.

All procedures that involve animals in USDA Pain Category Columns D or E are extensively reviewed during the protocol approval process. Prior to formal protocol review, a veterinarian with experience and/or training in laboratory animal medicine must review all procedures. In addition, the primary investigator must write a justification for all procedures for animals in Columns D and E. The DoD standard protocol states, "Procedures causing more than transient or slight pain that are unalleviated must be justified on a scientific basis in writing by the primary investigator. The pain must continue for only the necessary period of time dictated by the experiment, and then be alleviated, or the animal humanely euthanized." Moreover, the primary investigator must sign an assurance statement that alternative procedures are not available, and the Institutional Animal Care and Use Committee must review and approve all procedures before the study begins.

IV.2 RESULTS/DISCUSSION

IV.2.1 General Results

There was a total of 327,097 animals reported used in FY99, which is a 12% increase from FY98 and a 41% (226,603) decrease from FY93 (Figure IV-1). The Animal Welfare Act of 1985 defines animals as "any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal, as the Secretary may determine." Therefore, only 8% (26,340) of the animals reported used by the DoD in FY99 are considered USDA reportable species.

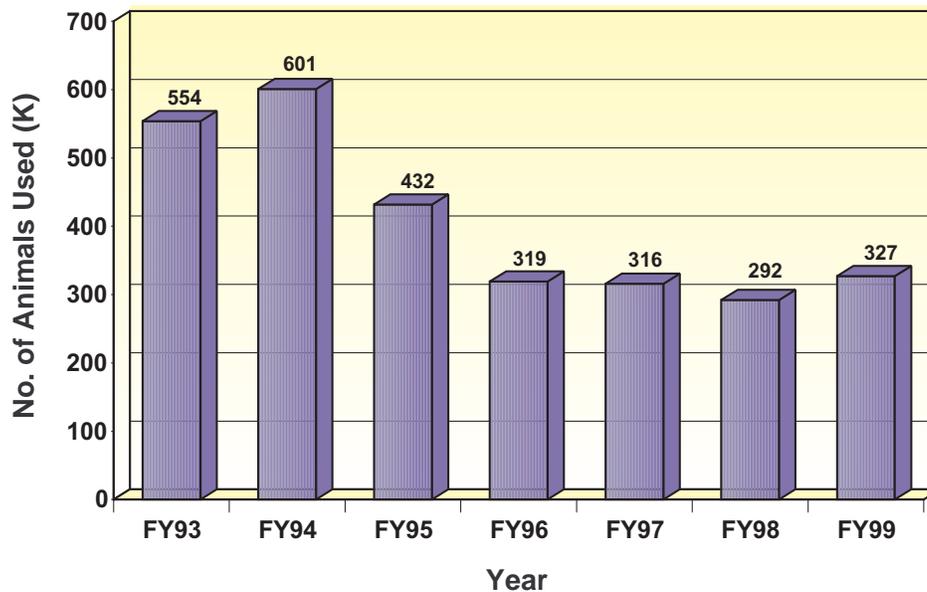


Figure IV-1 DoD Animal Use by Year

In FY99, 187,257 animals were reported used in intramural research programs and 139,840 were used in extramural grants or contracts (Figure IV-2). Reported intramural animal use increased by 23%, (34,433) in FY99 compared with FY98 use and decreased by 30% (80,834) compared with FY94 use. The intramural programs normally have less variation in their use of animals because they have a continuous mission and ongoing research in specific areas. In FY99 they experienced dramatic change in the use of animals due to the implementation of the Global Emerging Infectious Systems (GEIS) program. In the early 1990s, growing awareness and concern about the management of emerging infectious disease problems around the world led to meetings of public health experts sponsored by the National Academy of Sciences, by the World Health Organization/Pan American Health Organization, and by the White House. DoD

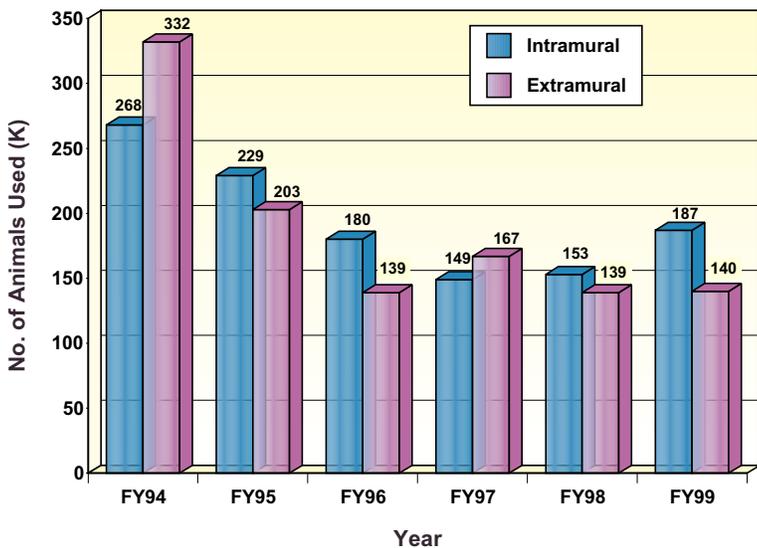


Figure IV-2 Intramural/Extramural Animal Use by Year

representatives participated in these discussions. One result was a Presidential Decision Directive NSTC-7 in June 1996 that formally directed all federal agencies to cooperate in surveillance and research on new infectious disease problems. Because of its wide-ranging assets for disease control, the mission of the DoD was expanded to support global surveillance, training, research, and response to emerging infectious diseases. President Clinton directed a centrally coordinated program that improved DoD epidemiological capabilities and involved both U.S. military treatment facilities and military medical research units in the United States and abroad.

While extramural programs by their very nature have large fluctuations in the number of animals used from year to year due to a different number of contracts and grants awarded; there was very little fluctuation between FY98 and FY99. The number of animals reported used in extramural research was 1% (1,113) higher in FY99 than the number in FY98 and 58% (192,752) less than the number used in FY94. Fluctuations in extramural animal use may result from several factors. First, many extramural research projects do not use animals at all while others only use animals during a portion of the proposed project (e.g., third year of project) and still others use animals throughout the entire project. In addition, the level of funding for extramural programs varies from year to year, thereby changing the total number of extramural projects. Some extramural research programs are congressionally mandated such as Breast Cancer, Gulf War Illnesses, Neurofibromatosis, and Osteoporosis Research Programs; their funding is dependent on yearly congressional appropriations.

IV.2.2 Animal Use by Service

Information concerning total reported DoD use of animals by each service is presented in Figure IV-3. Figures IV-4 and IV-5 show the intramural and extramural animal use by service, respectively.

In FY99, the Army used 62% of the total number of animals reported used by the DoD, 50% of the intramural animals, and 80% of extramural animals. There was a 4% decrease in the Army's reported intramural animal use and a 6% decrease in extramural animal use since FY98. The Army manages several congressionally directed research programs such as the Breast Cancer, Prostate Cancer, Neurofibromatosis, Bone Health, Neurotoxin, Defense Women's Health, and Gulf War Illnesses. These programs used the majority (70% or 77,790) of the Army's extramural research animals. The U.S. Army Medical Research and Materiel Command is the congressionally mandated Lead Agency for infectious disease and military dentistry research and the DoD Executive Agency for medical chemical and biological defense and nutrition studies. The number of animals the Army used in research on infectious diseases

TOTAL = 327,097

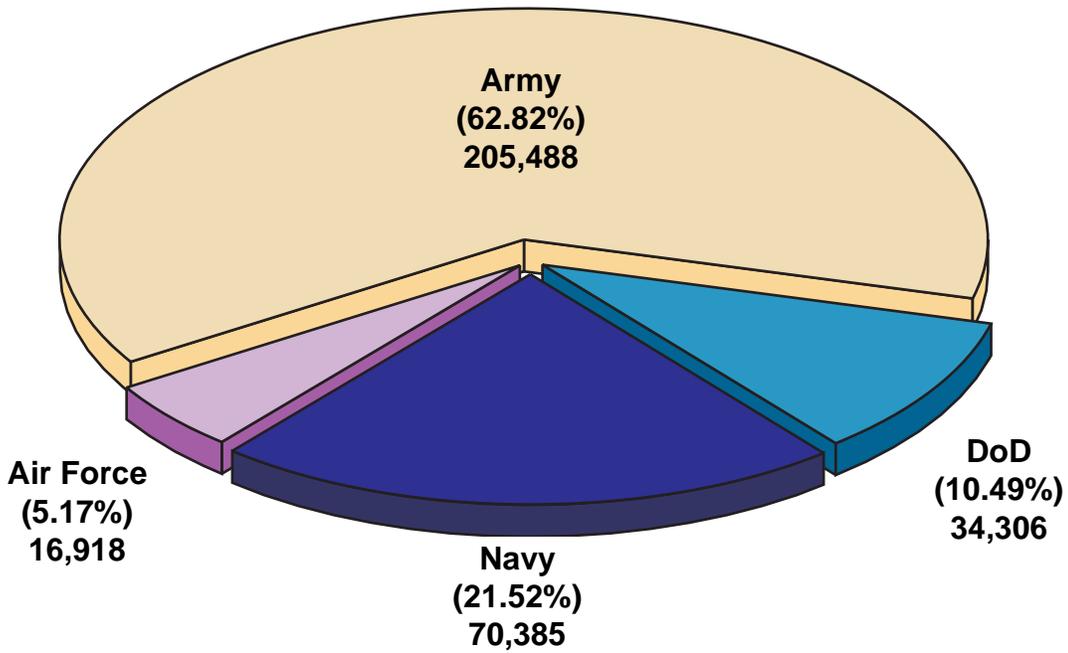


Figure IV-3 DoD Intramural and Extramural Animal Use by Service for FY99

TOTAL = 187,257

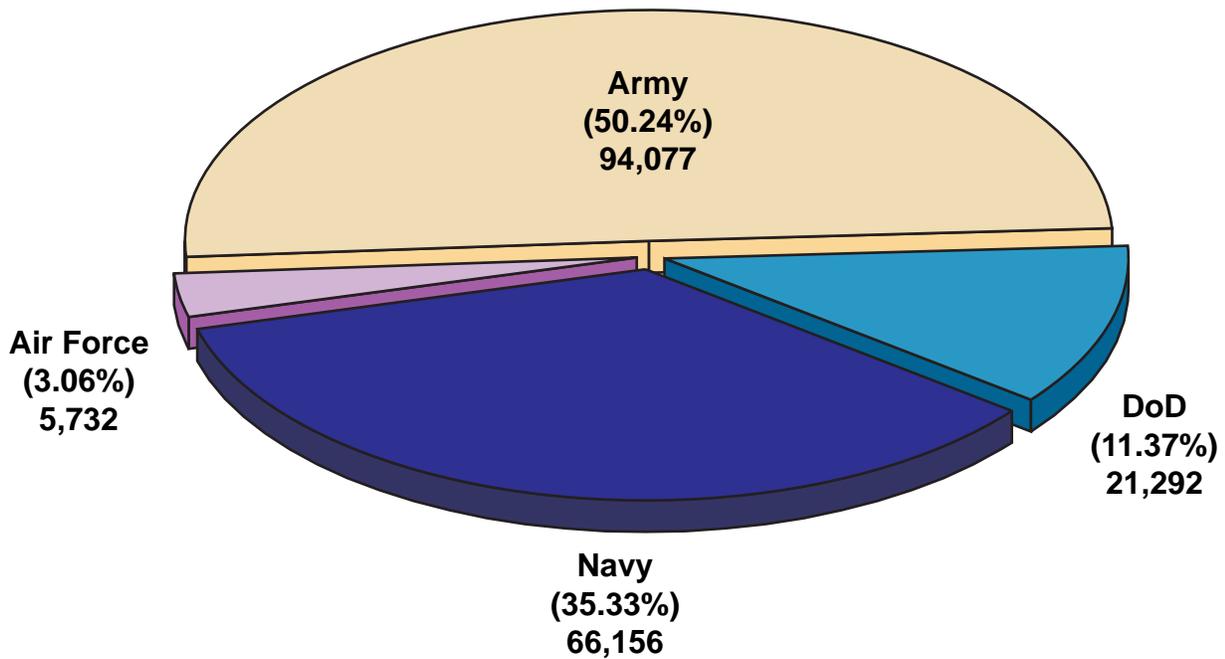


Figure IV-4 DoD Intramural Animal Use by Service for FY99

Percentages may not add up to 100% due to rounding of calculations

TOTAL = 139,840

Percentages may not add up to 100% due to rounding of calculations

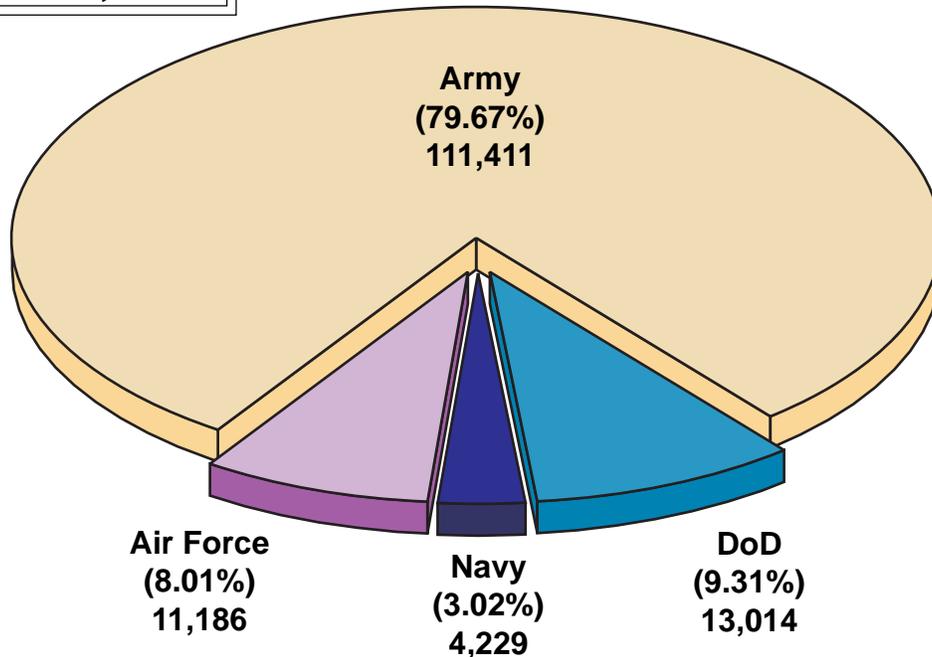


Figure IV-5 DoD Extramural Animal Use by Service for FY99

and chemical and biological defense was 34,821 and 63,327, respectively. Overall, the Army had a 2% decrease in animal use between FY98 and FY99 and has decreased its use of animals in research by 62% since FY94.

The Navy used 22% of the total number of animals reported used by the DoD, 35% of the intramural animals, and 3% of extramural animals. Comparing reported animal use in FY99 with use in FY98, there was a 62% increase in the total number of animals used by the Navy. This increase was in the Navy's intramural research projects, which increased by 69% (26,991). The Navy's extramural projects demonstrated a 0.6% decrease (24) in animal use.

The majority (84%) of the animals used by the Navy in FY99 were for research on infectious diseases. Ninety-eight percent of the animals used by the Navy in infectious disease research were rodents. The majority of the rodents were mice and were used in surveillance and research on new infectious diseases in the overseas research laboratories supporting the GEIS program. In support of the GEIS program, the Navy has increased its research in infectious diseases dramatically in FY98 and FY99 thus resulting in an increase in the Navy's overall use of animals in research and an increase in the DoD's total FY99 animal use.

The Air Force used 5% of the total number of animals reported used by the DoD, 3% of the intramural animals, and 8% of the extramural animals. The Air Force intramural animal use decreased by 888 and the extramural animal use increased by 7,494 resulting in a 6,606 overall increase in the number of animals used in research in FY99 compared with FY98. The Air Force used the majority (13,783) of its animals in nonmedical research projects.

The Office of the Secretary of Defense (OSD) components are the Uniformed Services University of the Health Sciences, Defense Advanced Research Projects Agency, Armed Forces Radiobiology Research Institute, and Armed Forces Institute of Pathology. OSD components used 11% of the DoD total animals used, 11% of the total intramural animals, and 9% of total extramural animals. There was a 17% (5,071) increase in the use of animals for the OSD components in FY99 compared with FY98. This increase was seen in both the intramural (4,970) and extramural (101) programs. The OSD components used the majority (92%) of their animals in clinical investigations (11,256) and medical research (20,509).

IV.2.3 Animal Use by Species

The DoD has developed three major classifications for reporting animal use: non-mammals, rodents, and other mammals. Compared with FY98, in FY99 there was a 26% (6,229) increase in the reported use of non-mammals and a 10% (1,087) increase in the number of other mammals used, with the bulk of this increase stemming from increases in the use of goats (236) and pigs (279). Rodents increased by 11% (28,230) (Figure IV-6) which was a 14% (30,563) increase in the use of mice, a 10% (2,821) increase in rats. At the same time, there were decreases in the use of chinchillas (29), gerbils (35), chipmunks (6), degus (13), guinea pigs (4,244), hamsters (533), and jirds (33). Once again this increase in rodents is linked with the GEIS program. The vast majority (96%) (280,426) of animals used by the DoD in FY99 were rodents, birds, amphibians, reptiles, and fish.

Since FY94, there have been significant decreases in the reported use of many species of animals by the DoD. There has been a 78% (109,012) decrease in non-mammals, a 36% (162,965) decrease in rodents, and a 12% (1,609) decrease in other mammals. Several animals used in

FY94 were not used at all in FY99 such as the fox, prairie dog, armadillo, civet, opossum, and mink. In addition, there have been significant decreases in the use of large animals such as marine mammals and horses. For example, between FY94 and FY99 there was a 56% (62) decrease in marine mammals and a 94% (99) decrease in horse use. At the same time, there were increases in the use of swine (856), rabbits (85), chinchillas (44), gerbils (28), ferrets (25), and reptiles (131). Overall, there has been a shift from the use of large animals to smaller animals and a shift to those that are lower on the phylogenetic scale.

In FY99, there was a slight increase in the combined use of nonhuman primates, dogs, and cats. When comparing FY98 with FY99, there was an increase in the use of nonhuman primates (193) and of dogs (181) and decrease in cats (8) (Figure IV-7). Nonhuman primates were primarily used in medical research (81%), and within medical research, the majority (52%) of nonhuman primates were used in the area of infectious diseases. The majority of dogs are used in medical research (63%) while most of the cats are used in training (78%).

Since FY94, there has been a 15% (332) decrease in the use of nonhuman primates and a 53% (585) decrease in the use of dogs and cats for research in the DoD. This illustrates the Department's continuing commitment to reducing the use of specific species in research.

DoD animal use by species is presented in Figure IV-8. Figures IV-9 and V-10 represent the intramural and extramural animal use by species for FY99.

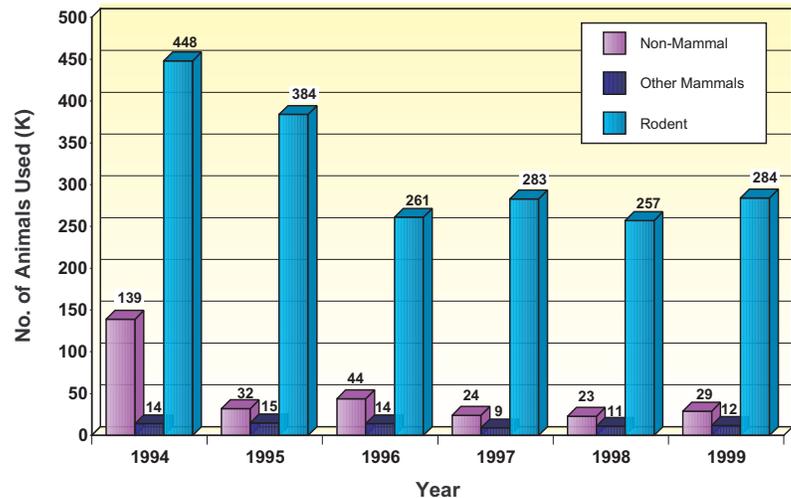


Figure IV-6 Decrease in Species

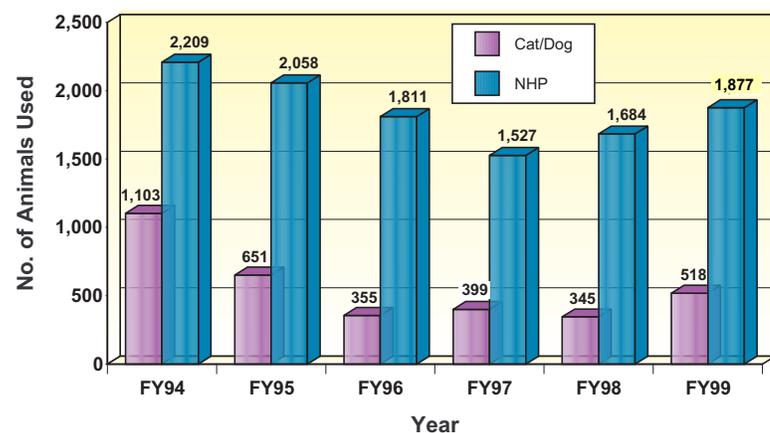
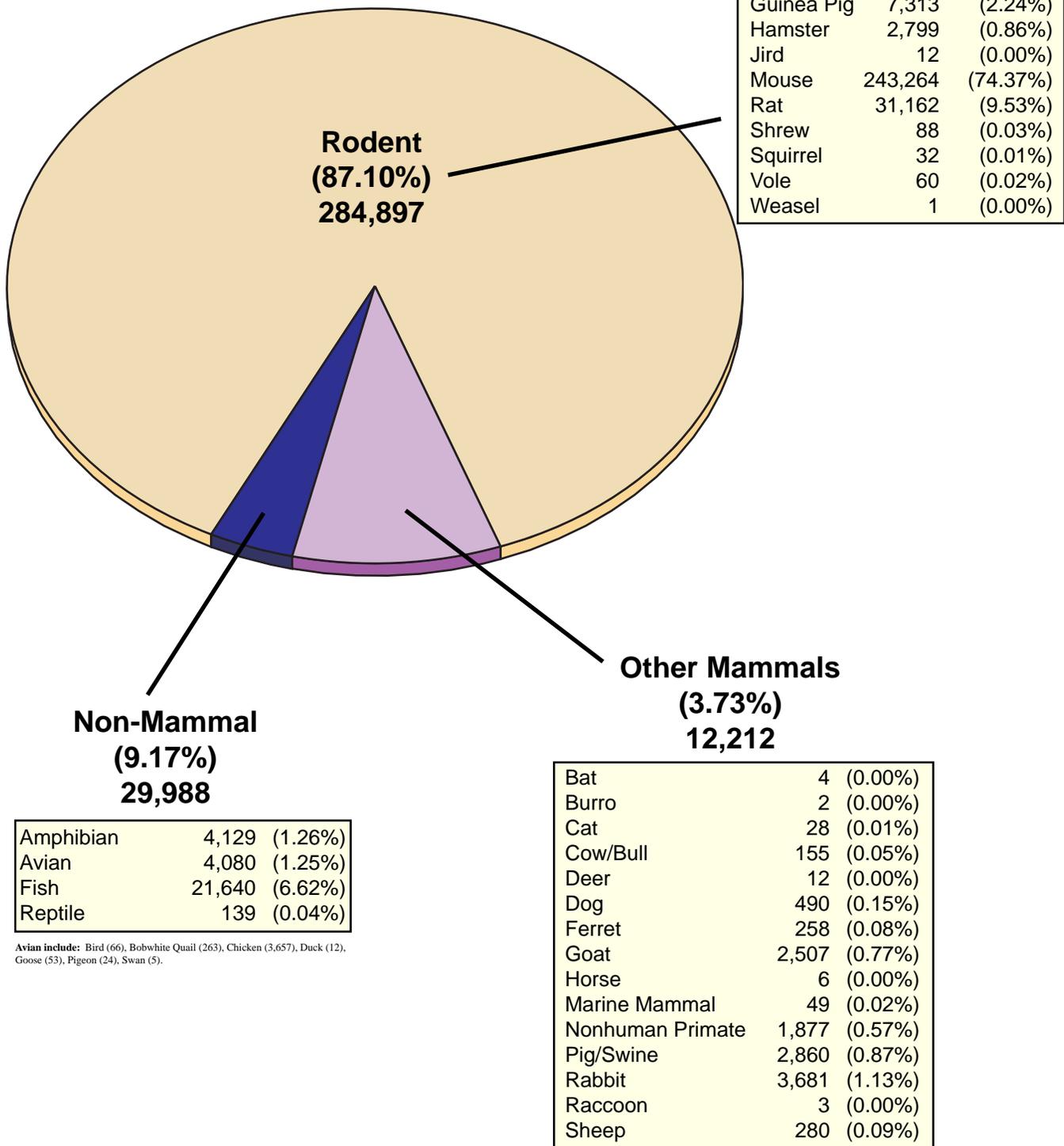


Figure IV-7 Use of Nonhuman Primates and Dogs and Cats by Year

TOTAL = 327,097



Avian include: Bird (66), Bobwhite Quail (263), Chicken (3,657), Duck (12), Goose (53), Pigeon (24), Swan (5).

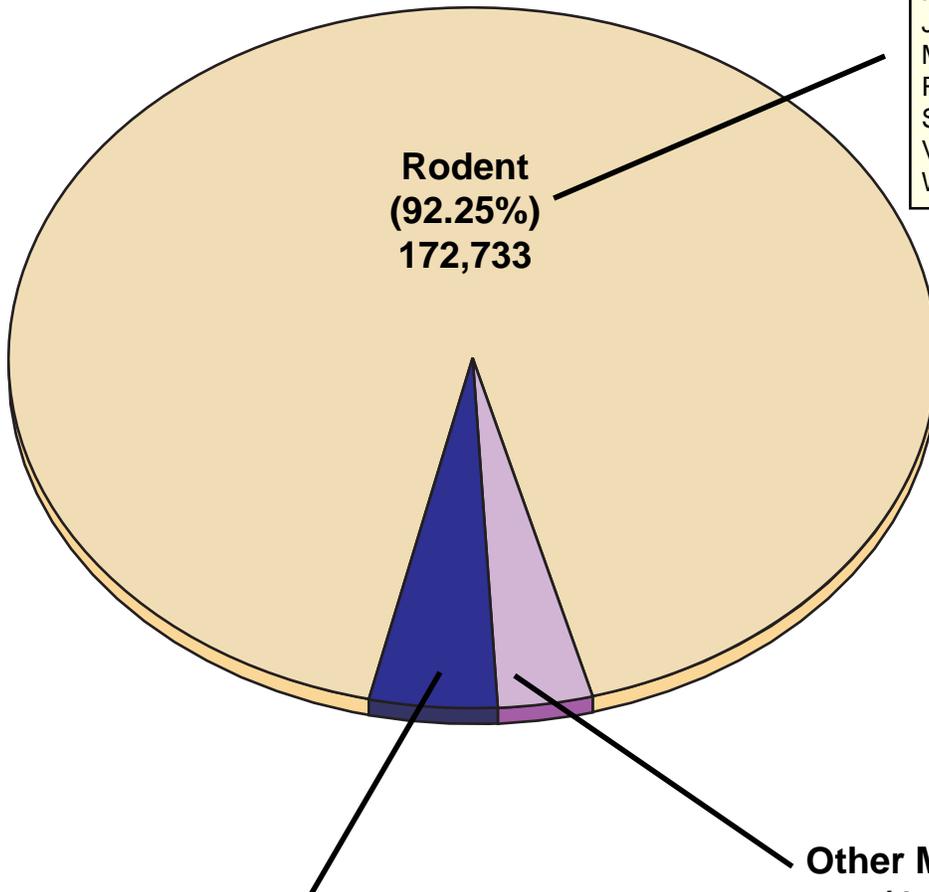
Marine Mammals include: California Sea Lion (2), Dolphin (38), Harbor Seal (1), North Elephant Seal (1), Sea Lion (4), Whale (3).

Percentages may not add up to 100% due to rounding of calculations

Figure IV-8 DoD Intramural and Extramural Animal Use by Species for FY99

TOTAL = 187,257

Chinchilla	71	(0.04%)
Chipmunk	1	(0.00%)
Gerbil	45	(0.02%)
Guinea Pig	4,132	(2.21%)
Hamster	2,522	(1.35%)
Jird	12	(0.01%)
Mouse	150,137	(80.18%)
Rat	15,664	(8.37%)
Shrew	88	(0.05%)
Vole	60	(0.03%)
Weasel	1	(0.00%)



**Non-Mammal (3.31%)
6,198**

Amphibian	393	(0.21%)
Avian	601	(0.32%)
Fish	5,200	(2.78%)
Reptile	4	(0.00%)

Avian include: Bird (66), Chicken (441), Duck (12), Goose (53), Pigeon (24), Swan (5).

**Other Mammals (4.45%)
8,326**

Burro	2	(0.00%)
Cat	28	(0.02%)
Cow/Bull	137	(0.07%)
Deer	12	(0.01%)
Dog	191	(0.10%)
Ferret	258	(0.14%)
Goat	2,481	(1.33%)
Horse	6	(0.00%)
Marine Mammal	45	(0.02%)
Nonhuman Primate	1,214	(0.65%)
Pig/Swine	2,126	(1.14%)
Rabbit	1,557	(0.83%)
Raccoon	3	(0.00%)
Sheep	266	(0.14%)

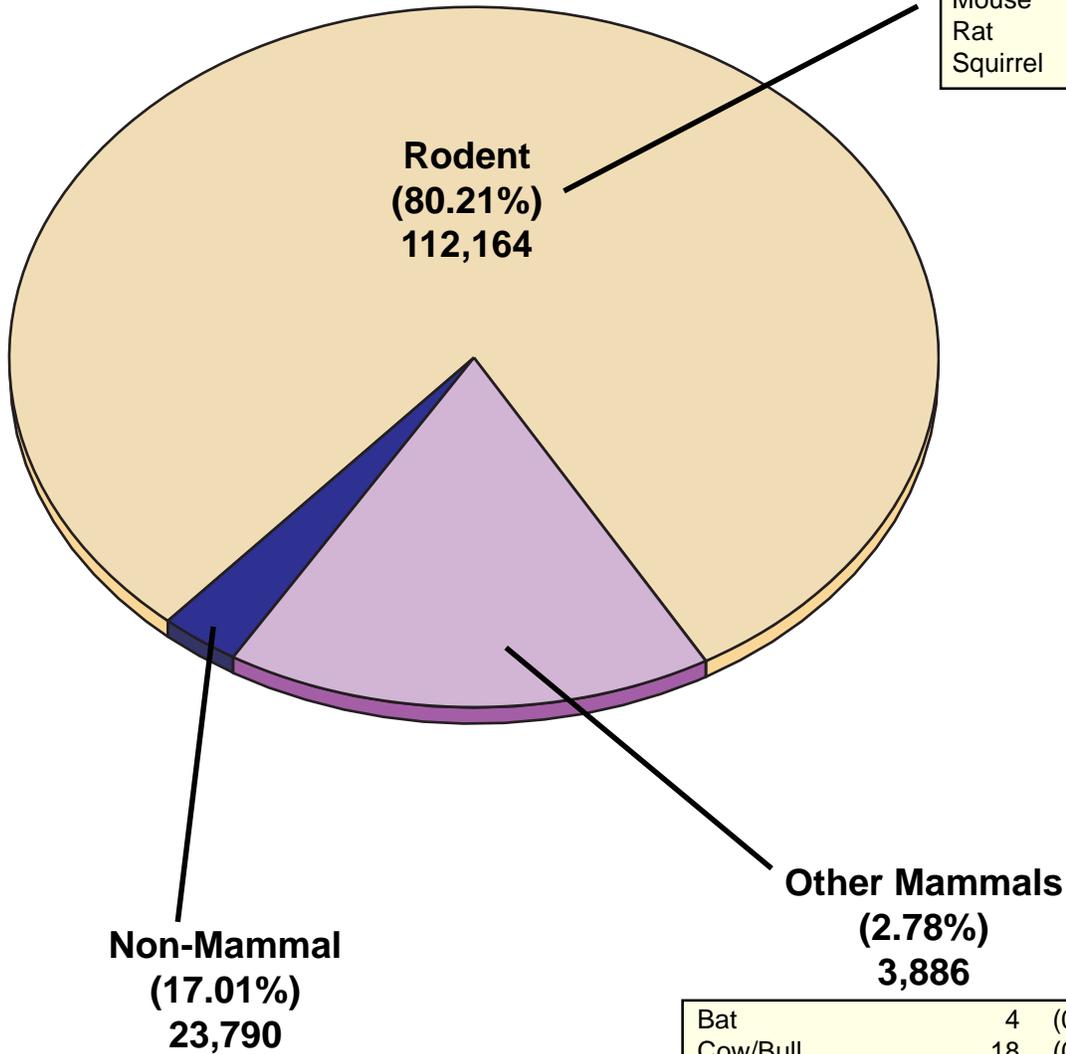
Marine Mammals include: Dolphin (38), Sea Lion (4), Whale (3).

Percentages may not add up to 100% due to rounding of calculations

Figure IV-9 DoD Intramural Animal Use by Species for FY99

TOTAL = 139,840

Chinchilla	37	(0.03%)
Degu	12	(0.01%)
Guinea Pig	3,181	(2.28%)
Hamster	277	(0.20%)
Mouse	93,127	(66.60%)
Rat	15,498	(11.08%)
Squirrel	32	(0.02%)



Amphibian	3,736	(2.67%)
Avian	3,479	(2.49%)
Fish	16,440	(11.76%)
Reptile	135	(0.10%)

Avian include: Bobwhite Quail (263), Chicken (3,216).

Bat	4	(0.00%)
Cow/Bull	18	(0.01%)
Dog	299	(0.21%)
Goat	26	(0.02%)
Marine Mammal	4	(0.00%)
Nonhuman Primate	663	(0.47%)
Pig/Swine	734	(0.53%)
Rabbit	2,124	(1.52%)
Sheep	14	(0.01%)

Marine Mammals include: California Sea Lion (2), Harbor Seal (1), North Elephant Seal (1).

Percentages may not add up to 100% due to rounding of calculations

Figure IV-10 DoD Extramural Animal Use by Species for FY99

IV.2.4 Animal Use by Category

Total reported animal use in the DoD by category is presented in [Figure IV-11](#), with the intramural and extramural breakouts in [Figures IV-12](#) and [IV-13](#), respectively.

The DoD has a critical and challenging mission: to discover, design, and develop military medical countermeasures against threats to the health and survivability of military personnel. In order to meet this mission, 83% of the animals used by the DoD in FY99 were in medical research. Forty-one percent (113,596) of the animals used in medical research were in the area of infectious diseases (M2) and of those, 98% (110,949) were rodents ([Appendix O](#)). The primary thrust of this research is the development of preventive measures against infectious disease through discovery, design, and development of prophylactic, therapeutic, and treatment drugs for relevant diseases. The chemical defense research program (M3)

TOTAL = 327,097

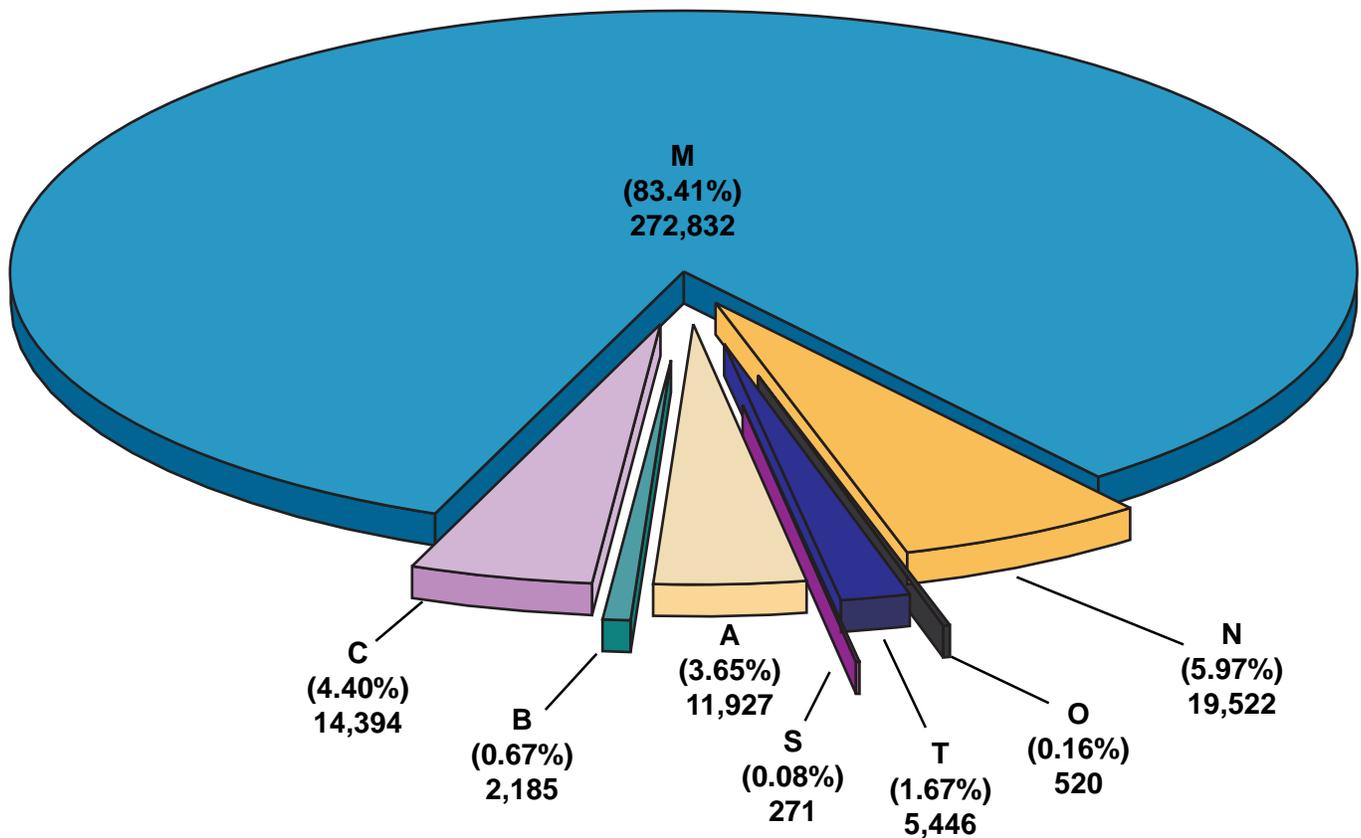


Figure IV-11 DoD Intramural and Extramural Animal Use by Category for FY99

A: Adjuncts/Alternatives to Animal Studies, B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E, N: Non-Medical RDT&E, O: Other Animal Use, S: Classified Secret or above, T: Training & Instructional.

Percentages may not add up to 100% due to rounding of calculations

TOTAL = 187,257

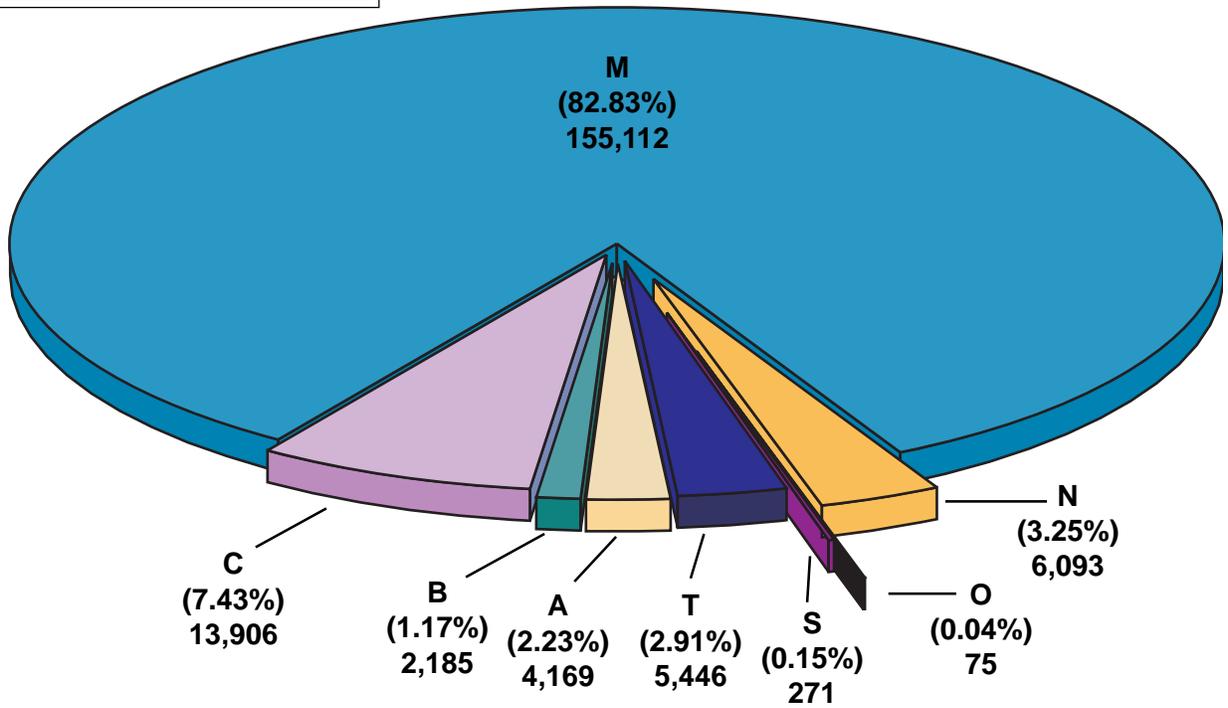


Figure IV-12 DoD Intramural Animal Use by Category for FY99

A: Adjuncts/Alternatives to Animal Studies, B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E, N: Non-Medical RDT&E, O: Other Animal Use, S: Classified Secret or above, T: Training & Instructional.

Percentages may not add up to 100% due to rounding of calculations

TOTAL = 139,840

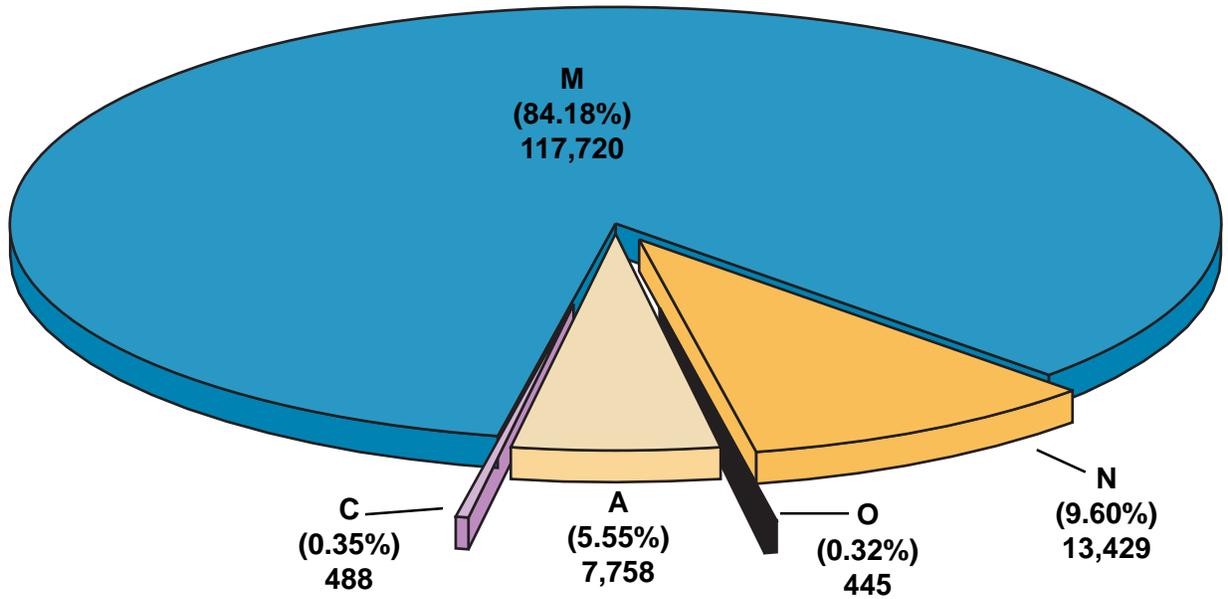


Figure IV-13 DoD Extramural Animal Use by Category for FY99

A: Adjuncts/Alternatives to Animal Studies, B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E, N: Non-Medical RDT&E, O: Other Animal Use, S: Classified Secret or above, T: Training & Instructional.

Percentages may not add up to 100% due to rounding of calculations

used 4% (11,127) and the biological defense research program (M4) used 19% (52,350) of the medical research animals. Medical biological defense develops, demonstrates, and fields new vaccines, drugs, and diagnostic kits for the prevention, treatment, and diagnosis of biological warfare agents. This research program protects the armed forces from the consequences of exposure to biological warfare agents and

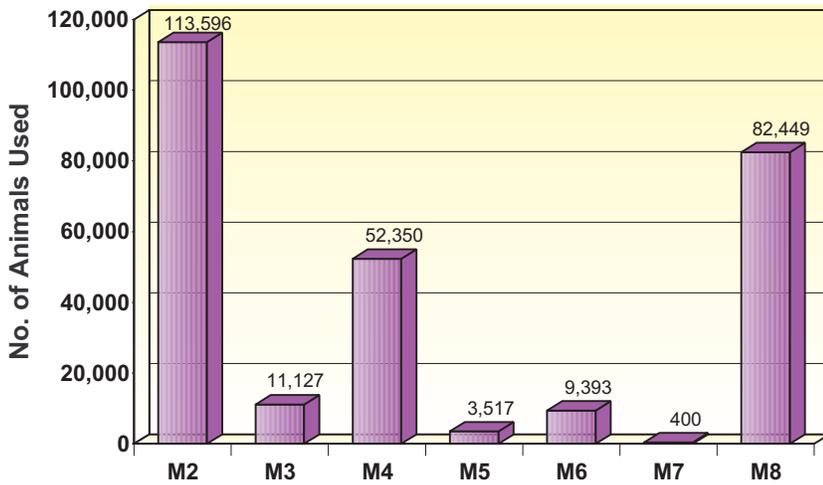


Figure IV-14 Animal Use by Medical Research Category

Research Category (M8)	No. of Animals Used	Percentage of M8
Biosample Protocol	116	0.14%
DARC Protocol	50	0.06%
Prostate Cancer Protocol	14,151	17.16%
Toxicological Testing	1,019	1.24%
Toxicology	1,368	1.66%
Zoonosis	1,133	1.37%
Bone Health	2,903	3.52%
Breast Cancer	51,507	62.47%
Defense Women's Health Research Program	78	0.10%
Disaster Relief And Emergency Medical Services	506	0.61%
Gulf War	1,066	1.29%
Medical Free Electron Laser	301	0.37%
Neurofibromatosis	2,560	3.11%
Neurotoxin	3,291	3.99%
Ovarian Cancer	2,400	2.91%
Total M8 Research	82,449	100.00%

Table IV-3 M8 (Other) Medical Research Category

enhances their survivability. M8 (Other Medical Research) accounted for 30% of the total medical research category (Figure IV-14). The Congressionally Directed Medical Research Programs in the areas of breast, ovarian, and prostate cancer, defense women's health, neurotoxin research, Gulf War illnesses, neurofibromatosis, and bone health used 77,956 animals. These programs accounted for 95% of M8 animals (Table IV-3), 29% of the animals used in medical research, and 24% of the total DoD animals used. These types of research programs can cause fluctuations in the total number of animals used from year to year depending on congressional funding levels and direction. Other areas of research within M8 are shown in Table IV-3.

Clinical research accounted for 4% (14,394) of the animals used by the DoD in FY99. Studies in this category address clinical medicine and surgical problems for the treatment of both diseases and combat casualties. Eighty-three percent of the animals used in clinical research were used in clinical medicine studies. While many of these conditions are unique to the military, several are not. Specific types of clinical studies are listed in Appendix N.

Two percent of the animals used by the DoD in FY99 were in the training, education, and instruction of personnel. Training and instruction are basically for animal technicians and medical personnel (Appendix N). Breeding stock, classified studies, and other studies each accounted for less than 1% of the DoD's total animal use in FY99.

Nonmedical RDT&E animal use increased by 57% (7,088) in FY99 and accounted for 6% of the total animal use. Research in the area of alternatives to the use of animals decreased by 30% (4,927) and accounted for 4% of the total animal use for FY99. Research in this category illustrates the Department's continuing initiatives to promote research to develop alternatives to reduce, replace, and refine the use of animals in DoD research. No animals were reported as used for offensive weapons testing during FY99.

IV.2.5 Animal Use by USDA Pain Category

Total reported animal use in the DoD by USDA pain category is presented in [Figure IV-15](#), with the intramural and extramural breakouts in [Figures IV-16](#) and [IV-17](#), respectively.

The majority (85%) of research in the DoD was not painful to the animals involved. In most cases (56%), the animals were not exposed to or involved in any painful procedures. In 28% of the cases, animals were given anesthesia or pain-relieving drugs during procedures that could have involved some pain or distress to the animals. In 15% of the animals used, anesthetics or analgesics were not used because they would have interfered with the validity of the results of experiments (Pain E category). A majority (86%) of the animals used in painful experiments (where reducing the pain or distress would have interfered with the validity of the results) were rodents. Fish accounted for 13% of the animals in USDA Pain Category E and other mammals accounted for less than 1% of animals in this pain category. Eight-five percent of the animals reported in USDA Pain Category E, were used in medical studies; of these, 76% of the animals were used in research on infectious disease and chemical and biological defense. Infectious disease and chemical and biological defense research falls into USDA Pain Category E because the animals have to be exposed to chemical or biological agents or antidotes or other infectious diseases or vaccines, which may result in some type of distress. There were no animals subjected to unalleviated pain during training studies.

The DoD clearly has a most diverse, unique, and demanding R&D mission. The modern battlefield is a hostile and dangerous environment with extraordinary potential for exposure to lethal or debilitating conventional weapons, exotic endemic diseases, biological and chemical agents, nuclear blast and radiation, directed energy sources, and complex and dangerous equipment. In addition, a host of adverse environmental conditions, such as cold, heat, high and low pressure, and G-forces are threats to service men and women. The DoD must provide acceptable protection against these threats and many others. The animals reported in USDA Pain Category E were used in research designed to find ways to protect service men and women from the threats they encounter daily. Note that in most of these studies the distress level is minor, such as in heat stress or gastrointestinal distress after being exposed to G-forces. This critical research is often reliant upon animal models for vaccine and efficacious countermeasure development. Research of this kind is not commonly done elsewhere in the government, academic, or private sectors and therefore is the sole purview of the DoD. Also, a large portion of these studies is driven by federal requirements, particularly those of the Food and Drug Administration.

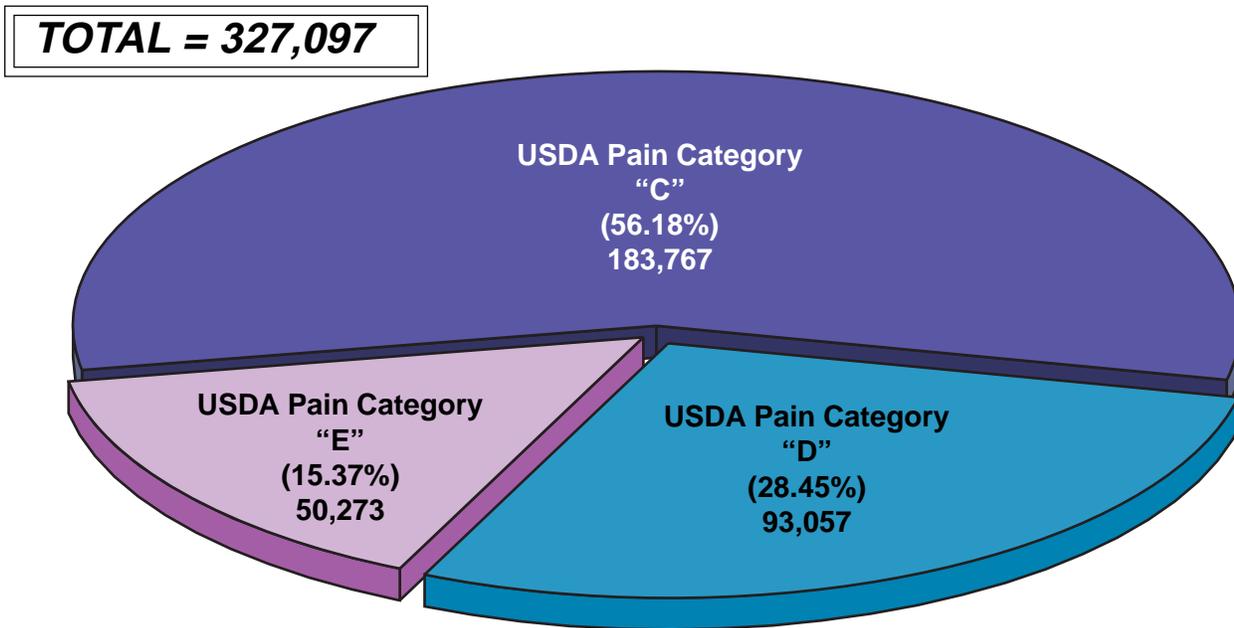


Figure IV-15 DoD Intramural and Extramural Animal Use by USDA Pain Category for FY99

Percentages may not add up to 100% due to rounding of calculations

TOTAL = 187,257

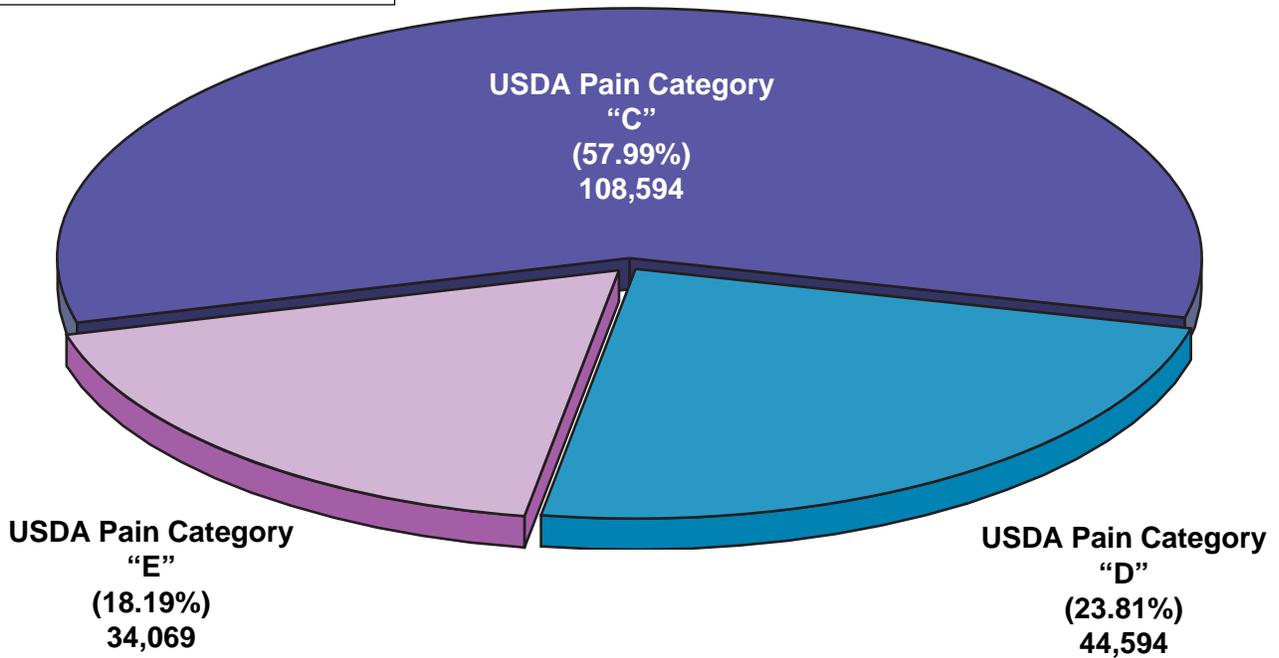


Figure IV-16 DoD Intramural Animal Use by USDA Pain Category for FY99

Percentages may not add up to 100% due to rounding of calculations

TOTAL = 139,840

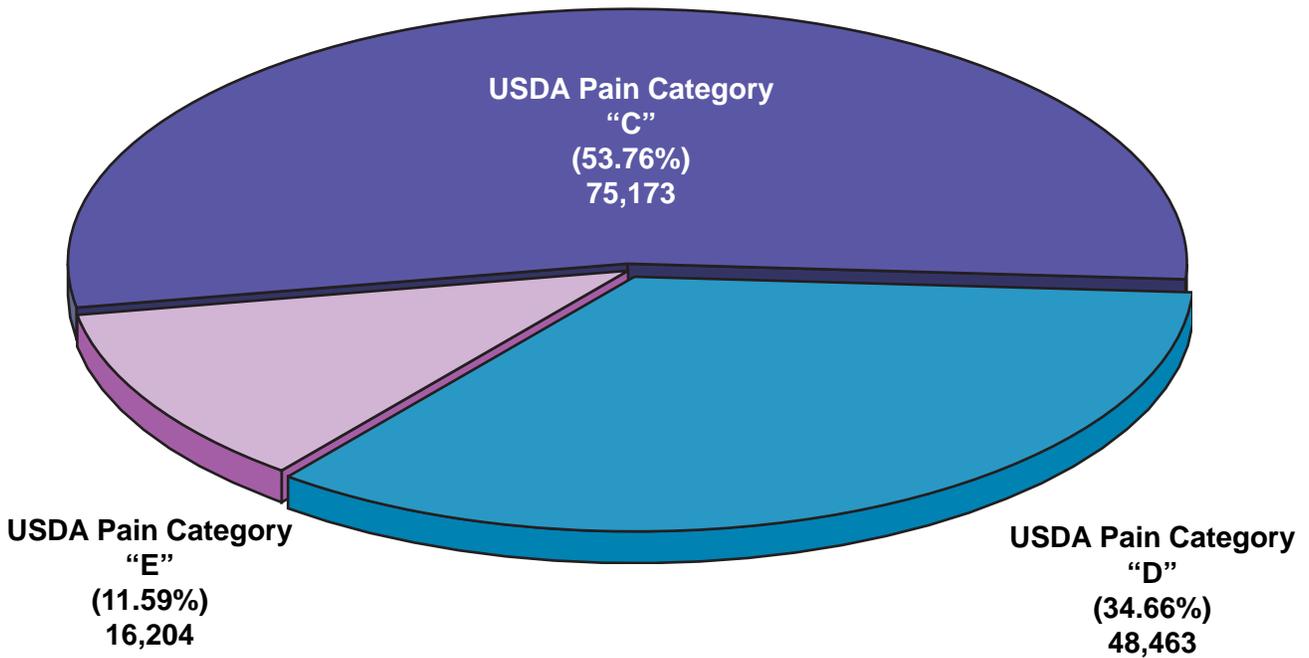


Figure IV-17 DoD Extramural Animal Use by USDA Pain Category for FY99

Percentages may not add up to 100% due to rounding of calculations

SECTION V

DoD INITIATIVES TO PROMOTE ALTERNATIVE METHODS THAT REPLACE, REDUCE, AND REFINES THE USE OF ANIMALS

Alternatives, as articulated in *The Principles of Humane Experimental Technique* (Russell and Burch, 1959), are defined as methods that Replace, Reduce, and Refine the use of animals. In addition to these Three Rs, the Department of Defense (DoD) advocates a fourth R, “Responsibility,” for implementing these alternative methods.

Replacement

The replacement alternative addresses supplanting animal use with nonliving systems, analytical assays, cell-culture systems, and with animals that are lower on the phylogenetic scale. Additionally, human subjects are used when experimental drugs and other procedures progress to human trials. Such trials are conducted in accordance with Title 32, U.S. Code of Federal Regulations, Section 219, “Protection of Human Subjects in DoD-Sponsored Research.”

Reduction

Decreasing the number of animals used through the use of statistical or innovative design strategies, while preserving the scientific integrity of the biological model, is a major emphasis of the reduction alternative to animal use.

Refinement

The refinement alternative for animal use addresses the need to ensure that the maximum humane use of each animal is obtained through proper protocol design and efficient utilization of animals, or through the modification of the experimental design to reduce the ethical cost associated with the study.

Responsibility

The DoD has taken responsibility for implementing animal use alternatives. This commitment illustrates the DoD’s initiative toward utilization and development of alternatives to animal use.

Department policy with regard to animal alternatives is promulgated in DoD Directive 3216.1, which directs that “it is DoD policy that... alternatives to animal species should be used if they produce scientifically satisfactory results....” This policy is implemented in the Joint Service Regulation on the Use of Animals in DoD Programs, which delegates responsibility to the local commander for utilization of alternatives to animals.

To illustrate the Department’s initiatives to promote these Four Rs, a description of such initiatives within DoD’s research laboratories and medical treatment centers is provided. The lists included in this section are not all inclusive, as the number of specific examples of implementing alternative methods that can be documented for DoD’s research projects is extensive. Rather, it illustrates the scope, diversity, and spirit of DoD’s Four Rs initiatives. This section will demonstrate a broad-based movement toward the use of biotechnology and other innovative adjuncts to replace and reduce animal use as well as refinement in methods used in essential animal studies.

V.1 DoD INITIATIVES TO PROMOTE ANIMAL ALTERNATIVES

The DoD has established a variety of initiatives and targeted programs that are currently in place to promote alternative methods that will replace, reduce, and refine the use of animals. These programs are designed to target individual and institutional awareness by providing educational opportunities, professional training, and fiscal resources toward implementing the Four Rs approach to animal use.

V.1.1 Science and Technology Objectives to Reduce Reliance on Animal Research

The DoD continues to seek alternatives to animal use through an Army Science and Technology Plan (STEP) initiated in FY93 and continuing through FY04 entitled “Reducing Reliance on Human and Animal Subjects of Research and Improving Experimental Conditions Using Animals.” The objectives of the STEP are to conduct basic research to develop new technologies to incrementally reduce future reliance on research animals. The U.S. Army Medical Research and Materiel Command’s Medical Biological Defense Research Program budgeted approximately \$524,000 in FY99 for this objective, which is available to support alternatives to animal use in research.

V.1.2 DoD-Sponsored Conferences and Workshops on Alternatives to Animal Use

The DoD promotes responsibility for alternatives to animal use by sponsoring major meetings and conferences on the subject. Every 2 years the DoD sponsors an international meeting on Alternatives to Animal Testing (Table V-1).

The 1992 meeting had 35 scientific platform sessions and 22 scientific poster presentations. This international symposium was attended by nearly 300 military and civilian scientists from four countries. Proceedings of the 1992 symposium are available through the Defense Technical Information Center (DTIC). In addition, in 1994 a book edited by Dr. Harry Salem titled *Animal Test Alternatives* was published by Marcel Dekker, Inc., which included chapters prepared by most of the presenters at this symposium. The 1994 meeting had 26 scientific platform sessions, including one by Dr. Martin Stephens of the Humane Society of the United States, and 45 scientific poster presentations. This meeting was attended by over 330 military and civilian scientists from seven countries. The proceedings and a monograph based on this successful symposium are available through DTIC. *Advances in Animal Alternatives for Safety and Efficacy Testing* was published by Taylor and Francis. The 1996 conference was coordinated

Table V-1 DoD-Sponsored Alternatives

Date	Title
1990	DoD Initiatives in Alternatives to Animal Testing
1992	Current Concepts and Approaches on Animal Test Alternatives
24-26 May 1994	Alternatives in the Assessment of Toxicity: Theory and Practice
12-14 June 1996	Biennial International Symposium on Alternatives in the Assessment of Toxicity Issues, Progress and Opportunities
December 1998	Alternative Toxicological Methods for the 21 st Century: Protecting the Human Health and Advancing Animal Welfare

with the Scientists Center for Animal Welfare, which held its meeting 10-11 June 1996 to present Animal Welfare and Toxicology/Safety Studies: Current Issues and Trends for the Next Century. In December 1998, the Alternative Toxicological Methods for the 21st Century: Protecting the Human Health and Advancing Animal Welfare conference was held in Bethesda, Maryland. This conference was sponsored by the Soldier and Biological/Chemical Command, the United States Army Center for Health Promotion

and Preventive Medicine, the United States Army Institute for Chemical Defense, and the National Institute of Environmental Health Sciences. The purpose of this conference was to present the latest research and trends in programs to replace, reduce, or refine the use of research animals.

V.1.3 National Research Council, Institute of Laboratory Animal Research, Educational Programs

The DoD's priority and continuing commitment to promoting individual and institutional responsibility for alternatives to animal use are reflected in continuing financial support of the Institute of Laboratory Animal Research (ILAR) educational program of the National Research Council. The principal thrust of the ILAR grant is development of institutional training materials, educational courses, and publications in support of the Department's laboratory animal care and use programs. This ILAR information is used in various military research facilities as an important adjunct to existing investigator training and technical education programs on animal care and use. The ILAR information and programs have generated strong animal alternative provisions for both civilian and military-specific research opportunities. The Department has funded this work since 1987 through 5-year grants, and is currently providing funding under the third such grant. In the face of diminishing research funds, the Department has resolved to maintain this important collaboration by providing in excess of \$130,000 annually for the ILAR program.

V.1.4 Institutional Animal Care and Use Committee Emphasis

Title 9 (Animals and Animal Products), Subchapter A (Animal Welfare), Parts 1-4 of the Code of Federal Regulations has specific provisions for addressing the issue of alternatives during the research animal protocol review process. The DoD has been a leader in forming lawfully constituted and functioning Institutional Animal Care and Use Committees (IACUCs) at its biomedical research facilities. Accordingly, DoD IACUCs consider alternatives to the proposed use of animals as an important review consideration. All DoD programs use a standardized IACUC protocol format ([Appendix E](#)) for animal use proposals, which requires that non-animal alternatives be considered. It states, "No study using animals should be considered prior to the elimination of all reasonable possibilities that the question might be adequately answered using other than animal means." Investigators must provide information on the animal model being proposed and justification for the selected species. The instructions for the standard protocol format states, "investigators should use the least sentient species that will permit the attainment of research objectives." In addition, the investigators are required to provide a short description of the features of the proposal that may qualify the study as one that replaces, reduces, or refines the use of animals. The DoD 1995 Policy Memorandum ([Appendix D](#)) requires that extramural contractor proposals utilizing animals in research, testing, or training include all the information contained in the DoD standard protocol format, thereby requiring them to also provide the alternatives information.

V.2 DoD PARTICIPATION IN OTHER FEDERAL ANIMAL ALTERNATIVE PROGRAMS

The DoD is also represented on the Interagency Regulatory Alternatives Group (IRAG), which planned and presented a "Workshop on Updating Eye Irritation Test Methods" in 1991 and another workshop on dermal testing held at the American College of Toxicology in November 1995. The DoD representative to the IRAG (Dr. Harry Salem) received the Food and Drug Administration's Group Recognition Award for his outstanding contributions to the IRAG ([Appendix Q](#)).

The National Institutes of Health Revitalization Act of 1993 (Public Law No. 103-43, Section 1301) directed the National Institute of Environmental Health Sciences of the National Institutes of Health (NIEHS/NIH) to establish an Applied Toxicological Research and Testing Program, which represents the NIEHS' component of the National Toxicology Program. The Act further directed the NIEHS to "(a) establish criteria for the validation and regulatory acceptance of alternative testing methods, and (b) recommend a process through which scientifically validated alternative methods can be accepted for

regulatory use.” To fulfill this mandate, an ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was established in 1994 by NIEHS. The mission of ICCVAM is to coordinate issues throughout the federal government that relate to the development, validation, acceptance, and harmonization of toxicological test methods. ICCVAM is responsible for the coordination of the development and review of various alternative toxicological methods. ICCVAM must also facilitate communication among all stakeholders in the development and review process of alternative methods. The ICCVAM evaluates proposals for alternative test methods and recommends further research. The ICCVAM comprises 38 members representing 14 different U.S. federal agencies. Members serve as points of contact and as sources to identify technical experts from their agencies to serve on specific topical workgroups. In FY99 the DoD had three representatives on the ICCVAM; Dr. Harry Salem (U.S. Army Edgewood Research Center), Dr. Robert Finch (U.S. Army Center for Environmental Health Development Laboratory), and Dr. John Frazier (U.S. Air Force DoD Tri-Service Toxicology Laboratory). The ICCVAM determines what assays warrant peer review, working groups, and test method workshops. When the members of the ICCVAM agree that an alternative method merits investigation, a working group is assembled. The working group in turn determines whether sufficient information exists for the assembly of either a peer review or a test method workshop. During FY99, there were three different working groups organized by the ICCVAM. In FY99, the DoD had representatives on two of the three working groups. Dr. Harry Salem and Dr. John Frazier served on the Corrosivity Working Group, which evaluated the Corrositex® assay. Dr. Robert Finch served on the Developmental Toxicology Working Group that evaluated Frog Embryo Teratogenesis Assay - Xenopus (FETAX). The results generated by ICCVAM’s working groups may be used to recommend U.S. federal regulations and/or guidelines for research.

Presentations have also been made on alternatives to the Board of Scientific Counselors of the National Toxicology Program of the National Institute of Environmental Health Sciences, Board of Scientific Counselors of the Food and Drug Administration, and Cancer Etiology Group at the National Cancer Institute.

V.3 DoD EXPERTISE AND TRAINING PROGRAMS THAT PROMOTE ANIMAL ALTERNATIVES

V.3.1 Veterinary Staff Expertise and Assistance Visits

The major biomedical research commands of the Military Departments each have credentialed laboratory animal medicine (LAM) veterinarians serving in key staff positions. In FY99 more than 35 board-certified specialists of the American College of Laboratory Animal Medicine (ACLAM) served in the DoD. In addition to being advisors to commanders on issues related to animal welfare and alternatives to animal use, these veterinarians provide oversight and structure to the command’s animal care and use programs. These officers also make periodic staff assistance visits to subordinate facilities that use animals and evaluate each laboratory animal care and use program. Consideration of the use of alternatives is reviewed on these staff assistance visits. Another important responsibility of the LAM veterinarian is to review extramural animal use protocols, ensuring that alternatives to animal use and personnel training issues have been addressed.

V.3.2 Professional Veterinary Training in LAM

The individuals who are specialty trained in veterinary LAM provide expertise in DoD biomedical research institutions, which strongly correlates to effective animal use alternatives programs. This is especially true in the critical area of refinements. The DoD has long been a leader in training veterinarians in the field of LAM, the biomedical and veterinary specialty most closely associated with laboratory animal welfare and laboratory animal care and use programs. Many of the nationally prominent leaders of several laboratory animal associations were formally trained in, or closely associated with, DoD LAM training programs. Examples are the current President of American Association for Laboratory Animal Science

(AALAS), the president elect of American Society of Laboratory Animal Practitioners (ASLAP), the current Secretary-Treasurer of ASLAP and ACLAM, and several past presidents of ACLAM. This traditional DoD strength in LAM expertise strongly enhances both animal care and use and animal alternatives programs. Of the 636 ACLAM members, 180 or 28% received some or all of their LAM training in DoD LAM training programs.

V.3.3 AALAS Technician and Laboratory Animal Science Training

There are a number of DoD research facilities that sponsor formal training programs leading to certification of animal care and research personnel as AALAS laboratory animal technicians. This specialized training is offered to both government and non-government animal technicians. It is an important mechanism for ensuring highly qualified animal care and research technicians in Defense laboratories. Individual DoD institutions have sponsored formal seminars for research personnel where experts from the National Agricultural Workshop present formal training and information on alternatives to animal use. In addition, Walter Reed Army Institute of Research (WRAIR) offers quarterly a workshop on ethical and administrative issues relating to animal use. The AALAS technicians' course curriculum and the WRAIR workshop curriculum include formal training and information on alternatives to animal use.

V.4 DoD DEVELOPMENT OF ANIMAL USE ALTERNATIVES

A review of the FY99 DoD research reveals that several DoD organizations were actively involved in the development of alternatives to animal use. These developments occur through research specifically designed to produce alternatives and to improve experimental techniques. Whenever possible, DoD investigators attempt to develop state-of-the-art, scientifically relevant, and reliable experimental procedures that can be performed without the use of animals. In addition, in cases where the animal models cannot be completely replaced, investigators work diligently to develop refinement techniques to reduce any stress placed on the animal during both experimental procedures and daily living. The DoD is very active in the development of alternatives to the use of animals in research. Below are examples of alternatives development that the DoD reported to be completed in FY99. This is only a sample of the alternatives development that was completed this year.

V.4.1 Alternatives Development Completed during FY99

Replacement:

Replacement with computer simulation, models, or other technologies

- An artificial eye has been developed that mimics the focusing characteristics of the real eye.

Replacement using *in vitro* cell cultures

- Development of systems to harvest osteoclasts from euthanized porcine bone marrow rather than from live mouse pups.
- Development of systems to harvest articular and meniscus cartilage from euthanized porcine carcasses from training labs for molecular phenotyping work.

Biochemical/physical methods

- Ascites production in mice will be replaced with bioreactors to produce large quantities of human monoclonal antibodies.

- In the development and application of RT-PCR for analysis of multiple *Bacillus anthracis* for improved vaccine, tissue culture technology has replaced the use of animals.
- In the development of DNA vaccines to prevent dengue, the cell lines are “immortalized” so that they may be passed many times in culture. Monoclonal antibodies made from hybridomas are used to minimize the numbers of mice required to produce antibodies as reagents.

Reduction:

Substitution of another animal species or the use of humans

- The use of guinea pigs reduces the number of rabbits and monkeys that would have to be used to investigate the effect of CpG oligonucleotides on specific and non-antigen-specific resistance to *B. anthracis* infection.

Substitution of computer simulation, models, or other technologies

- The characterization of recombinant bacterial superantigen vaccines, computer modeling and *in vitro* testing decrease the number of mice required.
- Microvascular Surgery Training Course, a compressed course schedule, reduced the number of animals used per course.

Utilization of alternative biological testing methods

- Development of a breast tumor cell that yields innate immune responses to mimic the effects of inflammation on mammary tumor cells *in vitro* and to screen for radiation and drug interactions reduces the number of mice required for research on nonionizing effects of radiation. This technology has a patent issued on it (U.S. Patent #6,013,520, 11 Jan 2000).
- Combining the lethality/safety studies with the efficacy studies of deglycosylated A-chain of ricin, a reduction of 360 mice is realized as compared to running the studies separately.
- A seizing neuronal culture model for the investigation of the mechanisms of hyperbaric oxygen toxicity reduced the number of rats from 15 - 20 to 1 per experiment.

Refinement:

Environmental enrichment

- Development of enhanced environmental enrichment by giving ferret colony a larger group holding area with more exploration accommodations.
- A unique housing pyramid was created using Vari-kennels. This enrichment environment offers multiple horizontal surfaces and “caves” that are frequently utilized by group-housed cats.

Increased training for animal technicians to increase skills

- Development of a “procedural practice” animal to optimally train principal investigators and histotechs in chinchilla ear anatomy and tissue processing characteristics using only one animal.
- Veterinary staff are trained by veterinarians in optimal intubation techniques resulting in more effective intubation techniques.

Reduce Pain and Distress

- Propagation of the Leishmania organism in the tail of the jird greatly reduces the apparent distress experienced by the subject.
- Use of radiotelemetry provides continuous monitoring, a noninvasive methodology (with the exception of the initial surgical procedure), and a large number of obtainable data.
- Use of fewer sarcoma cells per mouse decreases the likelihood of solid tumor production in adult mice, thus the amount of distress in these animals.
- Development of anesthetic regimens to provide more consistent/optimal depth of anesthesia, thereby reducing potential for anesthetic awareness/distress.

V.4.2 Alternatives Undergoing Development during FY99

As an ongoing process, the DoD is continuously developing alternatives. Below are examples of alternatives that were reported as currently in development by the DoD during FY99. This is only a sample of the alternatives being developed this year.

Replacement:

Replacement with computer simulation, models, or other technologies

- Development of computer models to determine trends in retinal damage. The models simulate the granular nature of the absorbers in the retinal tissue and agree with existing animal data.
- Computer models for target detection to replace dolphins are being developed.
- Sonar and signal processing methods to replace marine mammals are in development.

Replacement using *in vitro* cell cultures

- Interaction of liposomes with mouse macrophages is attempting to establish specific cell lines and clones which could replace live mice.
- Validation *in vitro* cell cultures, such as a culture of retinal pigmented epithelium cells, for use in research on ultrashort laser pulses.

Other species replace companion animals (dogs and cats)

- Determining the efficacy of hemostatic dosing in rat hip penetrating injury model to replace the dog model.

Non-mammalian species or species lower on the phylogenetic scale

- Development of a fish model to replace laboratory animals used in drinking water disinfection by-products studies.
- Modification of the Frog Embryo Toxicity Assay - Xenopus (FETAX) using metabolic activation (replacement for a common laboratory animal assay).
- Development of the adult frog model to support the reproductive toxicity program.
- Development of a murine model for the assessment of neuropathogenicity of nonhuman primate (NHP) herpes viruses.

- Evaluation of piglets as emetic models for staphylococcus enterotoxin-induced illness.
- Assessment of protection of antibody preparations against intoxication with botulinum neurotoxins.
- Development of a miniature pig model to replace the rhesus monkey retinal model used in retinal research.

Reduction:

Substitution of another animal species or the use of humans

- Development of an *in vivo* rabbit and *in vitro* bioassay system to evaluate candidate antimalarial drugs will decrease the number of NHPs used.
- The development of a guinea pig model to study Ebola virus pathogenesis will reduce the number of NHP studies needed to gain full understanding of Ebola infection in man.
- A rabbit model for anthrax is under development that will result in a reduction in the number of NHP needed for future studies.

Substitution of computer simulation, models, or other technologies

- Development of computer mathematical finite difference time domain calculations to predict the amount of energy absorbed by the NHP. Similar code is being developed for human dosimetry predictions and is validated by the NHP computer models.
- Development of a physiologically based pharmacokinetic model for ammonium perchlorate will reduce the number of animals required for studying this compound.

Utilization of alternative biological testing methods

- Establishment of T cell lines and clones that could replace live mice in the future.
- Laser-Doppler flowmetry multiple blood flow determinations can be made in a single rat that may reduce the number of rats required to look at traumatic brain injury.
- In epidemiology studies of viral hemorrhagic and encephalitic diseases, the time period animals are left in the field was modified from 1 month to 3-6 months, thus reducing by two-thirds the total number of animals used.

Refinement:

Environmental enrichment

- Development of environmental enrichment for NHP by engaging them in behavioral interaction that emulates the essential features of natural foraging. The results will be used to further refine the environmental condition of captive NHP and ensure their psychological well-being.
- Potential objects for environmental enrichment are being evaluated for many different animals.

Increased training for animal technicians to increase skills

- Development of training programs to teach research personnel the technical skills necessary to properly manage and humanely handle NHP during research experiments.

- Instruction in the care, handling, and management of rodents and lagomorphs.
- Development of veterinary techniques training programs for authorized personnel utilizing various laboratory animal species will result in better animal handling.

Reduce Pain and Distress

- Development of a nonsurgical animal model for ETEC diarrhea disease.
- Testing whether or not CO₂ anesthesia can be used without affecting the measured variables.
- Development of an alternative to death as an endpoint in scrub typhus infection, studies by using serology and temperature to determine appropriate time for euthanasia.
- Development of polyclonal antiserum against anthrax toxin components will serve as a potential replacement for Freund's adjuvant system with equally effective, but less reactive, adjuvant.
- Determination of a surrogate marker to predict death instead of going to death as an endpoint will reduce unnecessary stress.

V.5 DoD IMPLEMENTATION OF ANIMAL USE ALTERNATIVES

DoD research protocols strive to minimize the number of animals used to accomplish the program's mission and goals. During the review of protocols by the IACUC, investigators are specifically asked to present information indicating that "Reduction, Replacement, and Refinement" have been addressed in the animal study. Implementation of these alternatives reduces, replaces, and refines the Department's use of animals in research. This is accomplished by the implementation of both general and specific alternatives. In addition to the implementation of alternatives, the DoD has established policies specific to the refinement of animal use. For example, WRAIR has established a policy that mandates consideration of environmental enrichment for research animals. This policy allows for flexibility and creativity for improving conditions of laboratory animals.

General alternatives are those that are frequently implemented in many different DoD programs. Specific alternatives are those that may be specific to both a research protocol and/or facility. In FY99, 35 intramural institutions reported over 600 animal use alternatives that they were implementing. Six institutions with 26 projects reported eliminating the use of animals by the implementation of alternative methods. There are too many general and specific alternatives implemented by the DoD to present all of them in this report.

V.5.1 General Alternatives Implemented in FY99

The following examples are a representative listing of general alternative methods commonly practiced in DoD facilities:

Replacement:

- During the review process, all potential methods of adequately answering the research objective are reviewed prior to the use of an animal model.
- The evaluation process also considers the selection of a particular animal type; species lower on the phylogenetic scale are considered and used if their selection permits attainment of the research objectives.

- Non-animal training aids are used to replace the use of live animals.
- Computer simulations are used to replace live animals when scientifically possible.

Reduction:

- All animal use protocols are subject to review by a biostatistician who addresses the animal used, study design, and statistical evaluation packages, and ensures that the minimum number of animals will be used to meet the specific scientific objectives.
- Pilot studies are used to refine techniques and define the animal model so that animal use can be kept to the minimum required for statistical significance.
- Sharing of animal tissues with other investigators reduces animal use.
- Iterations of the experiments will be combined when possible to reduce the number of control animals used.
- Collaboration between DoD investigators allows for a single animal to be used in multiple training and research procedures and the sharing of control group information, resulting in an overall reduction in the number of animals used.
- Several types of data are collected simultaneously.
- Training sessions are designed to use the highest practical student-to-animal ratio.
- When possible, animals serve as their own controls.
- Studies are deliberately phased so they continue progress only if warranted.
- Advanced experimental designs are developed that can reduce the number of animals used.

Refinement:

- Parameters developed for early or alternative endpoints are used as experimental endpoints when possible.
- Animals are anesthetized before euthanasia to decrease stress.
- Moribund animals are humanely euthanized to prevent unnecessary pain or distress.
- Utilizing the environmental enrichment strategy, animals are housed in social settings (i.e., pairs or groups) in an enriched environment (e.g., nestboxes and toys).
- Animal handling skills and clinical techniques are taught to animal technicians, investigators, and research assistants to increase or ensure a proper skill level is attained prior to the start of a protocol.
- All Advanced Trauma Life Support training laboratory procedures are performed while the animals are under general anesthesia, and they are euthanized without regaining consciousness.

V.5.2 Specific Alternatives Implemented in FY99

Specific alternatives implemented by the DoD in FY99 were categorized as a subset of replacement, reduction, or refinement and are shown in [Table V-2](#). These categories illustrate the broad-based spectrum of alternatives to be implemented by the DoD. A representative listing of the specific alternatives is presented in [Appendix P](#).

Table V-2 Specific Alternatives Categories

Replacement:

- Non-mammalian species or species lower in the phylogenetic scale
- Biochemical/physical methods
- Computer simulations
- Other species replace companion animals
- Replacement using *in vitro* cell cultures

Reduction:

- Utilization of alternative biological testing method
- Substitution of computer simulations or other technologies
- Substitution of another species
- Enhanced protocol design

Refinement:

- Reduce pain
- Reduce distress
- Research models and animal alternatives
- Environmental enrichment and improved animal handling

V.6 SUMMARY

Each year new techniques and capabilities improve the handling, treatment, and use of animals in research and testing, and potentially reduce the need for animals in those same endeavors. In FY99, there was significant evidence of the DoD's aggressive pursuit to develop alternatives to replace, reduce, and refine the use of animals (for example, the alternatives currently being developed and those that have finished development are highlighted in [Section V.4](#)). In addition to these developmental efforts, animal use data for FY99 indicate the widespread implementation of validated alternatives. Fish are now replacing the use of mice and rats while rats and mice continue to replace nonhuman primates and other mammals higher on the phylogenetic scale in vaccine and drug development efforts. These and other examples of the development and implementation of alternatives have translated into reductions in the overall use of animals higher on the phylogenetic scale (see [Section V.4](#)). Animal use alternatives including reduction, replacement, and refinement constitute key initiatives in the biomedical research, testing, education, and training programs of the DoD. The number of large animals used by the military departments over the past decade has been significantly reduced, and some large species are rarely used at all. Dogs, cats, nonhuman primates, and marine mammals collectively represent less than 1% of the total animals used in research by the DoD.

SECTION VI

GLOSSARY

Adjuvant: An agent mixed in a vaccine to enhance the immunological protection afforded.

Alternatives to Animal Use: For purposes of this assessment, “alternatives” are defined as encompassing any subjects, protocols, or technologies that replace the use of laboratory animals altogether; reduce the number of animals required; or refine existing procedures or techniques so as to minimize the level of stress endured by the animal. These technologies involve the continued, but modified, use of animals; use of living systems; use of chemical and physical systems; and use of computers.

Analgesic: An agent that relieves pain without causing loss of consciousness.

Anesthetic: An agent that causes loss of the sensation of pain. Anesthetics may be classified as topical, local, or general.

Animal: For purposes of this assessment excluding embryos, animal is defined as any nonhuman member of 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). Under this definition, invertebrates are not included.

Animal Use: As any whole nonhuman vertebrate, living or dead, excluding embryos, that was used for research, development, test, and evaluation (RDT&E), clinical investigations, diagnostic procedures, and/or instructional programs. Only live animals or whole dead animals, as defined, that were either on hand in the facility or acquired during FY99 and used are included. Animal organs, tissues, cells, blood, fluid components, and/or byproducts purchased or acquired as such animal/biological components are not reported. This definition does not include animals used or intended for use as food for consumption by humans or animals, animals used for ceremonial purposes, or military working animals and their training programs.

Animal Welfare Act: This act, passed in 1966 and amended in 1970, 1976, and 1985, was originally an endeavor to stop traffic in stolen animals that were being shipped across state lines and sold to research laboratories. Amendments to the act have expanded its scope to include housing, feeding, transportation, and other aspects of animal care; however, the act bars regulation of the conduct of research and testing by the USDA.

Antibody: Proactive proteins produced by lymphocytes (a type of white blood cell) that can specifically bind foreign substances.

Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC): A voluntary private organization that has provided accreditation for over 600 institutions. AAALAC accreditation is based on the provisions of the National Research Council (NRC) *Guide for the Care and Use of Laboratory Animals*, and is recognized by the Public Health Service (PHS).

Biological Model: A surrogate or substitute for a process or organ of interest to an investigator. Animals or alternatives can serve as biological models.

Biomedical Research: A branch of research devoted to the understanding of life processes and the application of this knowledge to serve humans and animals. A major user of animals, biomedical research affects human health and the health care industry. It is instrumental in the development of medical products such as drugs and medical devices, and in the development of services such as surgical and diagnostic techniques. Biomedical research covers a broad spectrum of disciplines, such as anatomy, biochemistry, biology, endocrinology, genetics, immunology, nutrition, oncology, and toxicology.

Carcinogen: An agent or process that significantly increases the incidence of abnormal, invasive, or uncontrolled cell growth in a population. Carcinogens fall into three classes: chemicals, viruses, and ionizing radiation. A variety of screening assays have been developed to detect chemical carcinogens, including the *Salmonella*-mediated mutagenesis assay (Ames test), the sister chromatid exchange assay, and traditional laboratory animal toxicity tests.

Cell Culture: Growth in the laboratory of cells isolated from multicellular organisms. Each culture is usually of one type. Cell culture may provide a promising alternative to animal experimentation, for example, in the testing of mutagenicity, and may also become a useful adjunct in repeated-dose toxicity testing.

Computer Simulations: The use of specially devised computer programs to simulate cells, tissues, fluids, organs, and organ systems for research purposes: to develop mathematical models and algorithms for use in toxicity testing, and to simulate experiments traditionally done with animals for educational purposes.

Distress: Usually the production of pain, anxiety, or fear. However, distress can also occur in the absence of pain. For example, an animal struggling in a restraint device may be free from pain, but may be in distress. Distress can be eased with tranquilizers.

Guidelines for Animal Care and Use: Various organizations outside the federal government have adopted their own guidelines – e.g., the American Psychological Association’s *Guidelines for Ethical Conduct in the Care and Use of Animals*, which is comprehensive and has been endorsed by Federation of American Societies for Experimental Biology; the American Physiological Society’s *Guiding Principles in the Care and Use of Animals*; and the American Veterinary Medical Association’s *Animal Welfare Guiding Principles*. For federal guidelines, see Interagency Research Animal Committee, *NRC Guide for the Care and Use of Laboratory Animals*, and *PHS Policy*.

Institute of Laboratory Animal Research (ILAR): A component of the National Research Council, ILAR performs periodic surveys on the use of laboratory animals.

Institutional Animal Care and Use Committee (IACUC): An institutional committee that reviews research proposals and oversees housing and routine care of animals. The committee’s membership generally includes the institution’s attending veterinarian, a representative of the institution’s administration, users of research animals, and one or more nonscientist and lay member.

Invertebrate: Any nonplant organism without a spinal column, e.g., worms, insects, and crustaceans. Invertebrates account for 90% of the earth’s nonplant species. For the purposes of this assessment, invertebrates are not considered to be animals.

In vitro: Literally, in glass; pertaining to a biological process or reaction taking place in an artificial environment, usually a laboratory. Human and animal cells, tissues, and organs can be cultured in vitro. In vitro testing may hold some promising alternatives to animal testing, e.g., in testing for eye irritation and mutagenicity.

In vivo: Literally, in the living; pertaining to a biological process or reaction taking place in a living cell or organism.

National Research Council's *Guide for the Care and Use of Laboratory Animals*: Revised in 1996, the *Guide* details standards for animal care, maintenance, and housing. It is used by many animal research facilities, both within and outside the federal government. AAALAC and PHS also use it when assessing research facilities for accreditation.

Organ Culture: The attempt to isolate and maintain animal or human organs in *in vitro* culture. Long-term culture of whole organs is not generally feasible, but they can be sustained in cultures for short periods (hours or days).

Pain: Discomfort resulting from injury or disease. Pain can also be psychosomatic, the product of emotional stress. Pain can be induced by mechanical, thermal, electrical, or chemical stimuli, and it can be relieved by analgesics or anesthetics.

Protocol: The written plan of a scientific experiment or treatment.

Public Health Service *Policy on Humane Care and Use of Laboratory Animals*: Revised in 1986, the *Policy* applies to PHS-supported activities involving animals [including those of the National Institutes of Health (NIH)]. It relied on the NIH *Guide for the Care and Use of Laboratory Animals* (1985), and uses institutional committees for the assessment of programs and maintenance of records.

Reduction: Considered an alternative to animal use when fewer animals are used in research and education through changed practices, sharing of animals, or better design of experimental protocols.

Refinement: An alternative to animal use by better use and modification of existing procedures so that animals are subjected to less pain and distress. Examples of such refinements are the administration of anesthetics and tranquilizers, humane destruction, and the use of noninvasive imaging techniques.

Replacement: An alternative to animal use, replacing methods using animals with those that do not. Examples include the use of a placenta instead of a whole animal for microsurgical training, the use of cell cultures instead of mice and rats, the use of non-living systems, and the use of computer programs.

Research Facility: Under the Animal Welfare Act, any individual, institution, organization, or postsecondary school that uses or intends to use live animals in research, tests, or experiments. Facilities that receive no federal support for experimental work and that either purchase animals only within their own state or that maintain their own breeding colonies are not considered research facilities under the act.

Testing: Standardized procedures that have been demonstrated to predict certain health effects in humans and animals. Testing involves the frequent repetition of well-defined procedures with measurement of standardized biological endpoints. A given test may be used to evaluate many different substances and use many animals. Testing is used to establish the efficacy, safety, and toxicity of substances and procedures.

Tissue Culture: The maintenance *in vitro* of isolated pieces of a living organism. The various cell types are still arranged as they were in the original organism and their differential functions are intact.

Veterinary Medicine: The science and art of prevention, cure and/or alleviation of disease and injury in animals. Veterinary medicine includes the management of animal care and use programs.

SECTION VII

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