

**Report to the Committees on Armed Services of the Senate and  
House of Representatives**

**on**

**Department of Defense Animal Cost  
and Use Programs 1993**

# Table of Contents

	<u>Page</u>
List of Figures.....	vi
List of Tables.....	vii
List of Acronyms.....	xi
Section I	Introduction ..... I-1
	I.1. Requirements for Use of Animals in the DoD ..... I-1
	I.2. DoD Policy Governing Animal Research ..... I-2
	I.3. Scope of Report ..... I-3
	I.3.1. Accreditation of DoD Laboratories by AAALAC ..... I-3
	I.3.2. Service and DoD Animal Use in Research, Education, Training and Testing, and the Cost of Animal Based Programs vs. Other Research Programs ..... I-4
	I.3.3. DoD Initiatives to Promote Alternative Methods that Replace, Reduce, and Refine the Use of Animals .... I-5
	I.3.4. Animal Use Oversight and Procedures to Avoid Unintended Duplication of Research and Unnecessary Research..... I-5
Section II	Accreditation of Defense Department Laboratories by the American Association for Accreditation of Laboratory Animal Care ..... II-1
Section III	Service and DoD Animal Use in Research, Education, Training and Testing, and the Cost of Animal-Based Programs vs. Other Research ..... III-1
	III.1. Methods ..... III-1
	III.2. Results ..... III-1
Section IV	Defense Department Initiatives to Promote Alternative Methods that Replace, Reduce and Refine the Use of Animals .IV-1
	IV.1. Responsibility ..... IV-2
	IV.1.1. Science and Technology Emphasis on Alternatives to Animal Subjects of Research ... IV-2
	IV.1.2. Conferences and Workshops on Alternatives to Animal Use ..... IV-2
	IV.1.3. National Research Council, Institute of Laboratory Animal Resources (ILAR), Educational Programs ..... IV-3
	IV.1.4. Institutional Animal Care and Use Committee (IACUC) Emphasis ..... IV-3
	IV.1.5. Veterinary Staff Expertise and Assistance Visits ..... IV-3

## Table of Contents (cont)

	<u>Page</u>
IV.1.6. Professional Veterinary Training in LAM.....	IV-4
IV.1.7. AALAS Technician and Laboratory Animal Science Training .....	IV-4
IV.2. DoD Initiatives to Replace, Reduce and Refine the Use of Animals .....	IV-5
IV.2.1. Replacement .....	IV-5
IV.2.1.A. Replacement using biochemical or physical methods .....	IV-5
IV.2.1.B. Replacement using computer simulations .....	IV-5
IV.2.1.C. Replacement using in vitro cell culture .....	IV-6
IV.2.1.D. Replacement with non-mammalian species .....	IV-6
IV.2.1.E. Replacement with human tissue or volunteers .....	IV-6
IV.2.1.F. Replacement with discarded tissue from other laboratories or food processing plants .....	IV-7
IV.2.2. Reduction.....	IV-7
IV.2.2.A. Reduction by use of alternative screening methods to study efficacy in biological testing .....	IV-7
IV.2.2.B. Reduction by substitution of in vitro or ex vivo methods .....	IV-9
IV.2.2.C. Reduction by substitution of another species of animal or human volunteers .....	IV-10
IV.2.2.D. Reduction by substitution of computer simulations or other technologies...	IV-10
IV.2.3. Refinement .....	IV-11
IV.2.3.A. Refinement to protocols that reduce pain .....	IV-11
IV.2.3.B. Refinement to protocols that reduce distress .....	IV-12
IV.2.3.C. Refinement in research models and animal alternatives .....	IV-13
IV.3. Summary.....	IV-13
Section V Animal Use Oversight and Procedures to Avoid Unintended Duplication of Research and Unnecessary Research .....	V-1

## Table of Contents (cont)

	<u>Page</u>
V.1. Determination of Department of Defense (DoD) Needs for Animal Research.....	V-1
V.2. Oversight of Animal Care and Use Facilities.....	V-2
V.2.1. Military Departments Agencies .....	V-2
V.2.2. IACUC.....	V-3
V.2.3. AAALAC.....	V-5
V.2.4. Community Visits .....	V-5
V.2.5. Additional Oversight.....	V-5
V.3. Chain of Command Over Animal Care and Use Facilities.....	V-6
V.4. Avoidance of Unintended Duplication of Research .....	V-6
V.4.1. Less Formal Disincentives for Unintended Duplication of Research .....	V-7
V.5. Avoidance of Unnecessary Research .....	V-8
V.6. Summary.....	V-8
Section VI Glossary.....	VI-1
Section VII References (in order of citation).....	VII-1

## List of Figures

	<u>Page</u>
Figure III-1	Total DoD Intramural and Extramural Animal Use by Branch ..... III-3
Figure III-2	Total DoD Intramural and Extramural Animal Use by Species FY93 ..... III-4
Figure III-3	Total Army Intramural and Extramural Animal Use by Species FY93 ..... III-5
Figure III-4	Total Navy Intramural and Extramural Animal Use by Species FY93 ..... III-6
Figure III-5	Total Air Force Intramural and Extramural Animal Use by Species FY93 ..... III-7
Figure III-6	Total Tri-Service DoD Facility Intramural and Extramural Animal Use by Species FY93 ..... III-8
Figure III-7	Total DoD Intramural and Extramural Animal Use by Category.. III-9
Figure III-8	Total Army Intramural and Extramural Animal Use by Category ..... III-10
Figure III-9	Total Navy Intramural and Extramural Animal Use by Category ..... III-11
Figure III-10	Total Air Force Intramural and Extramural Animal Use by Category ..... III-12
Figure III-11	Total Tri-Service DoD Facility Intramural and Extramural Animal Use by Category ..... III-13
Figure III-12	Total DoD Intramural and Extramural Species Use by Category ..... III-14
Figure IV-1	DoD Intramural Total Animal Use FY87-93..... IV-1
Figure V-1	DoD Technology Area Responsibilities..... V-7
Figure V-2	Structure of Armed Services Biomedical Research, Evaluation, and Management Committee ..... V-7

## List of Tables

### Page

Table I-1	Examples of DoD Materiel Products that Require Animal Use .....	I-2
Table I-2	Summary of DoD Animal Use Statistics.....	I-4
Table I-3	Examples of DoD Initiatives for Replacement, Reduction, and Refinement of the Animals Used in Research .....	I-5
Table III-1	Costs of Animal Use Programs Relative to Total Research, Education, Training, and Testing Programs - Army .....	III-15
Table III-2	Costs of Animal Use Programs Relative to Total Research, Education, Training, and Testing Programs - Navy .....	III-19
Table III-3	Costs of Animal Use Programs Relative to Total Research, Education, Training, and Testing Programs - Air Force .....	III-21
Table III-4	Costs of Animal Use Programs Relative to Total Research, Education, Training, and Testing Programs - Tri-Service DoD Facilities.....	III-23
Table III-5	DoD Costs of Animal Use Programs Relative to Total Research, Education, Training, and Testing Programs.....	III-25

## List of Acronyms

AAALAC	American Association for Accreditation of Laboratory Animal Care
AALAS	American Association of Laboratory Animal Science
APA	American Psychological Association
APS	American Physiological Society
ASBREM	Armed Services Biomedical Research Evaluation and Management
ASD(HA)	Assistant Secretary of Defense (Health Affairs)
ASTMP	Army Science and Technology Master Plan
AVMA	American Veterinary Medical Association
BAA	Broad Agency Announcement
DDR&E	Director, Defense Research and Engineering
DoD	Department of Defense
DTIC	Defense Technical Information Center
ELISA	Enzyme Linked Immunosorbent Assay
FDA	Food and Drug Administration
FY	Fiscal Year
G	Gravity
IACUC	Institutional Animal Care and Use Committee
IG	Inspector General
ILAR	Institute of Laboratory Animal Resources
JCAHO	Joint Commission for Accreditation of Health Organizations
JDL	Joint Directors of Laboratories
JTCG	Joint Technology Coordinating Groups
LAM	Laboratory Animal Medicine
NIH	National Institutes of Health
NMR	Nuclear Magnetic Resonance
OIG-DoD	Office of the Inspector General, Department of Defense
OSD	Office of the Secretary of Defense
QLIS	Quantitative Luminescence Imaging System
RDT&E	Research, Development, Test, and Evaluation
RFR	Radiofrequency Radiation
S&T	Science and Technology
SCID	Severe Combined Immunodeficiency Disease
SEB	Staphylococcus Enterotoxin B
SF	Special Forces
STO	Science and Technology Objective
TAPSTEM	Training and Personnel Systems Science and Technology Evaluation and Management
USAMRDALC	U.S. Army Medical Research, Development, Acquisition, and Logistics Command (Provisional)
USDA	United States Department of Agriculture
WRAIR	Walter Reed Army Institute of Research

## SECTION I INTRODUCTION

---

---

The National Defense Authorization Act for Fiscal Year 1993, Report of the House Armed Services Committee, H.R. 5006, May 19, 1992, requested the Secretary of Defense to provide a comprehensive annual report to the Committees on Armed Services of the Senate and House of Representatives on animal cost and use programs. This report has been prepared in accordance with the specific requirements described in the committee report (HASC Report #102-527, page 151). The report covers all animal research conducted by the Department of Defense (DoD) including education, training, and testing both in DoD laboratories and by extramural projects funded by the Department for Fiscal Year 1993.

### **I.1. REQUIREMENTS FOR USE OF ANIMALS IN THE DoD**

The continued use of animals by the DoD in research, education, and training is absolutely essential to ensure sustained technological superiority of U.S. warfighting capabilities. The DoD's animal use programs ultimately translate into maintaining and improving military readiness, force structure and modernization. They contribute directly to ensuring that deployed service men and women may best attain an early and decisive victory with minimum casualties. Additionally, humanitarian benefits of the DoD investment in animal research are shared on an international basis to improve the quality of life of both humans and animals.

Although many alternatives to animal use have been discovered and applied by the Department, there remain situations in which there are no acceptable alternatives. While fundamental scientific and biomedical principles have been explored and understood using non-living and cell culture models, the complex interactions within the human (e.g., organ, endocrine, circulatory and related systems) and with the environment have not been effectively modeled for all areas of concern to the DoD. For example, disease has been and remains a major cause of death and disability in military conflicts. During Operations Desert Storm and Restore Hope, outbreaks of shigellosis and other diarrheal diseases, leishmaniasis and other parasitic diseases, and malaria continued to threaten the health and well being of our troops.

As a consequence, DoD must develop the materiel and technological means to best protect and sustain the health and well being of service men and women despite battle and disease-non-battle threats, and to provide the best medical treatment possible to those who become casualties. This responsibility underlies, for example, the need for DoD to conduct research, and to train and educate military health-care providers in the most effective medical management of battlefield casualties. Unlike medical counterparts found in civilian emergency medicine and trauma management, battlefield health care must very often be provided in an austere, harsh and hostile environment hours away from a definitive care hospital. Whereas an urban 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 only by a single aidman and the medical supplies he can carry.

Another visible area requiring DoD to use animals in research is the need to develop vaccines and drugs to protect, sustain and treat service men and women during military operations. Like health-care delivery, these research programs are focused on the disease causing threats most important to the military missions. Ethical concerns as well as the regulatory requirements of the Food and Drug Administration (FDA) necessitate that candidate vaccines and drugs be demonstrated to be safe in both laboratory and animal models prior to initiation of human studies. The statutory basis for such ethical and FDA regulations is the legitimate concern of ensuring human protection from dangerous and ineffective treatments. Indeed, during the final stages of vaccine and drug development, large-scale testing is conducted using human volunteers, often individuals who are naturally exposed to the disease in question. Table I-1 is a representative list of drugs, vaccines and other future products from DoD research that critically depend on using animal subjects.

## I.2. DoD POLICY GOVERNING ANIMAL RESEARCH

While essential to the protection of military personnel, animal research is considered a trust. The DoD has consistently adhered to direction (DoD Directive 3216.1, "The Use of Animals in DoD Programs") to follow the most stringent Federal regulations that govern the use of animals in order to prevent unnecessary suffering and to minimize the numbers of animals used. All animal research must conform to requirements of the 1966 Animal Welfare Act (P.L. 89-544) as amended in 1976 (P.L. 94-279) and 1985 (P.L. 99-198), as well as the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*, (fifth edition, 1985, NIH86-23) and the requirements of the applicable regulations of the United States Department of Agriculture (USDA). Although the Animal Welfare Act does not apply to mice of the genus *Mus* and rats of the genus *Rattus*, the DoD voluntarily conducts research with these exempt species with the same procedures defined in the Animal Welfare Act for

### Products Available for Use

Japanese Encephalitis vaccine  
 Insect/Arthropod repellent lotion  
 Rift Valley fever killed vaccine  
 Eastern & Western Equine Encephalitis vaccines  
 Venezuelan Equine Encephalitis vaccine  
 Pyridostigmine Nerve Agent Pretreatment  
 Skin decontaminating kit, M291  
 Convulsant antidote for nerve agent  
 Mefloquine, antimalarial  
 Halofantrine, antimalarial  
 Medical aerosolized nerve agent antidote

### Products in Advanced Development

Malaria vaccines - blood stage  
 Diarrheal Disease Vaccines: *Shigella*, enterotoxigenic  
*E. coli*, *V. cholera*, *Campylobacter*  
 Hepatitis A vaccine  
 Botulinal Toxoids & antitoxins  
 Meningococcal Group B vaccine  
 Vaccinia-vectored Korean Hemorrhagic fever vaccine  
 Argentine hemorrhagic fever vaccine  
 Q-fever vaccine  
 Tularemia live vaccine  
 Smallpox vaccine, cell culture derived  
 Rift Valley fever live vaccine  
 Chikungunya fever vaccine  
 Antimalarial drugs WR238,605 & WR6026  
 Topical skin protectant for chemical agents  
 Microencapsulated antibiotic, ampicillin, dental  
 Hypertonic saline dextran  
 Nerve agent antidote, multichambered autoinjector  
 Schistosome topical antipenetrant  
 Nerve agent antidote system (HI-6)  
 Antimicrobial dermal dressing

### Candidate Products for Advanced Development

Topical antileishmanial lotion  
 Azithromycin antimalarial drug  
 Botulinum toxoid heptavalent  
 Ricin toxoid  
 Staphylococcal Enterotoxin B toxoid  
 Saxitoxin Countermeasure  
 Rapid Bioagent ID system, fiber optic biosensor  
 Malaria Sporozoite Vaccine

Table I-1 Examples of DoD Materiel Products that Require Animal Use

other mammals. At the same time, DoD biomedical researchers have aggressively developed novel procedures to replace, reduce, and refine the use of animal subjects during experimentation.

### **I.3. SCOPE OF REPORT**

This report is a thorough review of animal use in research, education, training and testing in the DoD. It was prepared by a panel of veterinarians and scientists involved in animal research and training and individuals involved in the oversight of animal care and use from each of the three services. The report is divided into seven sections including this introduction. This report includes: information on Accreditation of DoD laboratories by the American Association for Accreditation of Laboratory Animal Care (AAALAC) (Section II); Service and DoD animal use in research, education, training and testing; and, the cost of animal based research vs. other research cost (Section III); DoD initiatives to promote alternative methods that replace, reduce, or refine animal use (Section IV); and animal use oversight procedures to avoid unintended duplication of research or unnecessary research (Section V); glossary (Section VI); and a list of references in order of citation (Section VII). Several appendices are included that provide more detailed information to support these sections.

#### **I.3.1 Accreditation of DoD Laboratories by AAALAC**

DoD animal use facilities are reviewed in Section II. All DoD laboratories that conduct animal research will be required to apply for AAALAC accreditation; 60% of DoD laboratories already have received accreditation, a record that exceeds the average for civilian research laboratories registered with the USDA. Animal use programs in the DoD strive to meet all the requirements of AAALAC. However, the age of many DoD animal research facilities predates many of the current engineering standards and is an obstacle to full AAALAC accreditation. Certain laboratories are awaiting renovation or construction of new facilities to meet AAALAC standards for physical housing. Despite the physical limitations of some facilities, all laboratories are required to establish rigorous animal husbandry programs to provide the best possible housing and care of research animals. In keeping with the spirit of the Animal Welfare Act and guidance from AAALAC, limitations of older buildings and mechanical systems do not necessarily imply that research animals are exposed to unhealthy conditions. Such facilities require more intense animal husbandry programs to care for the animals and often require the added expense of sophisticated housing that provides a sanitary microenvironment for the animals. DoD invites AAALAC inspection of all facilities and programs to ensure that the best possible care is provided to DoD animals, regardless of the constraints of the physical facilities. The recently completed Inspector General report on animal use in DoD facilities confirmed the effectiveness of animal husbandry programs in DoD facilities and concluded that although not all facilities were AAALAC accredited, animals in DoD facilities were maintained in healthy environments and treated humanely. As stated in the report, "The inspection teams were completely satisfied with the health and welfare of the animals in DoD research facilities. ... All the personnel assigned the care of the

animals were competent, interested, and committed to the humane care of the animals."

### I.3.2 Service and DoD Animal Use in Research, Education, Training and Testing, and the Cost of Animal Based Programs vs. Other Research Programs

A profile of DoD animal use and costs is provided in Section III. During 1993, the cost of animal-based research, development, testing evaluation (RDT&E) was approximately 0.4% of the total expenditure for RDT&E. As a result of various new methods to replace animal models, the number of animals used in intramural DoD research has declined 40% from 1987 to 1993. DoD policy (DoD Directive 3216.1, "The Use of Animals in DoD Programs") specifically prohibits the use of nonhuman primates in development work for nuclear, biological, or chemical offensive weapons. This policy has been extended to include dogs or cats; and, no dogs or cats may be used for the purpose of training students or other personnel in surgical or other medical treatment of wounds produced by any type of weapon. In addition, in 1969 the United States biological warfare program was terminated by Executive Order, and subsequently the offensive chemical warfare program has been abolished. The vast majority of the expense of biomedical research with animals has been for development of vaccines and drugs for the prevention and treatment of diseases or the toxic effects of biological and chemical weapons that have become an increasing threat to our forces. Table I-2 summarizes the major animal use statistics for DoD research.

<u>Total Animal Use by Agency</u>			No. of Animals	% of Total
DoD Total			553,700	
Tri-Service			77,331	14
Army			417,626	75
Navy			36,102	7
Air Force			22,705	4
<u>Total Animal Use by Species</u>			No. of Animals	% of Total
Mice			366,700	65
Rats			52,769	9
Guinea Pigs			9,981	2
Hamsters			8,747	2
Rabbits			4,862	1
Goats			2,787	<1
Pigs			2,170	<1
Nonhuman Primates			2,210	<1
Dogs			735	<1
Ferrets			307	<1
Cats			211	<1
Sheep			383	<1
Other mammals			7,366	1.3
Avians			1,050	<1
Other nonmammals			93,754	17
<u>Total Animal Use by Category</u>			No. of Animals	% of Total
Medical RDT&E			417,062	75
Non-Medical RDT&E			80,424	14
Clinical Investigation			24,590	4
Adjuncts/Alternatives			22,945	4
Training & Instructional			8,380	2
Breeding Stock			299	<1
Offensive Weapons Testing			0	0
<u>Total Animal Use Cost</u>				
	Animal-Based Program Cost	Total Cost of Programs	% of Cost in Animal Use Programs	
RDT&E	\$157,698K	\$37,560,016K	0.4	
Education	\$21,732K	\$87,947K	25	
Training	\$309K	\$2,076K	15	

Table I-2 Summary of DoD Animal Use Statistics

### 1.3.3 DoD Initiatives to Promote Alternative Methods that Replace, Reduce, and Refine the Use of Animals

DoD efforts to replace, reduce, and refine the use of animals in research are reviewed in Section IV. Animal research is an essential part of the scientific process, but it is always undertaken after due consideration of alternatives. Each protocol that proposes to use animals in research or training must explain the need for whole 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 because of ethical considerations and other inherent benefits. One DoD organization, the U.S. Army Medical Research, Development, Acquisition and Logistics Command (Provisional), has established a major Science and Technology Objective to develop replacement, reduction, and refinement strategies for the use of animals in research. This objective has an annual budget of approximately \$600,000. The DoD sponsors conferences and workshops to promote alternatives to animal research. The DoD sponsors a five year grant with the Institute of Laboratory Animal Resources of the National Research Council to develop institutional training materials, education, and publications in support of DoD laboratory animal care and use programs. The Institutional Animal Care and Use Committee (IACUC) process also includes a strong emphasis on consideration of alternatives in all new protocols. Table I-3 describes several examples of new procedures that greatly replace, reduce and refine the use of animals.

Innovative statistical techniques have been developed to reduce the numbers of animals and to replace the classical LD<sub>50</sub> test.

An *in vitro* screening test for drugs to treat malaria has been developed under contract that conserves 4,000 mice per year.

Microsomal homogenate from one rat liver allows 30 experiments and saves 29 animals for each 30 experiments for a total annual savings of 2,300 rats.

A number of protocols now pool control animals across experiments or use historical controls to save on total animal use.

*In vitro* culture of the malaria parasite in human blood cells serves as a source for genetic material to advance the development of a vaccine for malaria.

*In vitro* test using peripheral blood from humans has been developed to test the effectiveness of a Staphylococcal Enterotoxin B toxoid, replacing the use of primates.

Rodent and swine models are being developed to replace the use of nonhuman primates in studies of disease.

Cell culture *in vitro* methods have been developed for passage of disease-causing viruses.

Neuronal cell cultures are used to study the mechanisms of nerve cell injury *in vitro* and to screen for new drugs for neuronal protection against toxins and traumatic injury.

Video tapes are used for adjunct training of technicians and investigators for common animal use procedures, ie., venipuncture, handling, restraint, etc.

**Table I-3 Examples of DoD Initiatives for Replacement, Reduction, and Refinement of the Animals Used in Research**

### 1.3.4 Animal Use Oversight and Procedures to Avoid Unintended Duplication of Research and Unnecessary Research

DoD animal use oversight is reviewed in Section V. All DoD facilities and extramural institutions sponsored by the DoD must submit all proposed uses of animals to an IACUC. Forty of forty-five DoD operated animal use sites have established their own IACUC to review all proposed animal uses to ensure compliance with the Animal Welfare Act; of the five sites without an IACUC, three sites have such low animal use that they submit their protocols to their parent organization

for review; one site is collocated at Wright-Patterson Air Force Base and uses its IACUC; and one facility does not use live animals in its research. The goal of the IACUCs is to strike a reasonable balance between the requirements for animal welfare, the benefits of animal use for advancing solutions to important DoD problems, and the concerns of the community. DoD Directive 3216.1 specifies that DoD IACUCs shall conform to the provisions of the Animal Welfare Act. Each IACUC serves as an independent decision-making body of the institution and establishes policy for the care and use of animals at that facility in accordance with applicable DoD Directives, Federal law and regulations. They review all proposed animal uses as described in detailed protocols. The protocol 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 specifies the procedures to be used with the animals, the methods to avoid or minimize pain, the qualifications of all persons conducting procedures with the animals, and the disposition of the animals at the termination of the work. The IACUC ensures that all personnel using animals 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 all significant deficiencies. The IACUC enforces compliance with the procedures specified in the protocols by conducting inspections and by hearing and investigating reports of deviation from approved procedures. Finally, the IACUC serves as an impartial investigator of reports of violations of good animal practices and is empowered to suspend the use of animals for investigations not conducted in accordance with Animal Welfare Act or institutional policy.

All DoD IACUCs include an outside member who is not affiliated with the facility and is specifically charged with the responsibility to provide a community perspective on all proposed animal uses. The outside member can perform unannounced site visits and participates in all discussions and votes on all protocols. Non-affiliated members come from a variety of backgrounds including biologists, chaplains, homemakers, health-care professionals of various specialties, veterinarians, and non-technical professions. The non-affiliated member is invited to participate in introductory and continuing training to ensure that they are fully knowledgeable of the requirements for humane care and treatment of animals.

Responsibility for oversight of the Department's science and technology programs rests with the Director, Defense Research and Engineering (DDR&E). Her staff, in conjunction with representatives from the Services, annually review all 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 and Evaluation Management (ASBREM) Committee, which was created by Congressional direction in 1981. The ASBREM is co-chaired by the DDR&E and the Assistant Secretary of Defense (Health Affairs). The overall

biomedical effort is carefully integrated and scrutinized for duplication of effort by seven subordinate joint technology coordinating groups reporting to the co-chairpersons.

In conclusion, it is the policy of DoD that all animal utilization will be conducted in full compliance with the Animal Welfare Act. Use of animals in research is essential to protect the health and lives of Servicepersons, and DoD will be engaged in biomedical research that involves the use of animals for the foreseeable future.

## SECTION II

# ACCREDITATION OF DEFENSE DEPARTMENT LABORATORIES BY THE AMERICAN ASSOCIATION FOR ACCREDITATION OF LABORATORY ANIMAL CARE

---

---

This section responds to the Committee's request that the Secretary of Defense explain why all Department of Defense (DoD) laboratories are not accredited and to move toward accreditation of all DoD laboratories. Since June 1, 1984, with the publication of the Joint Regulation on *The Use of Animals in DoD Programs* (Appendix A), the DoD has 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 DoD programs. It also covered transportation, care, use, review, reporting, and other animal husbandry areas for animals used in: research, development, test, and evaluation (RDT&E); clinical investigation; diagnostic purposes; and instructional programs or exhibitions in the Military Departments and Defense Agencies. Importantly, The Joint Regulation exceeds statutory requirements in that it requires all DoD organizations having animals (other than for military working, recreational, and ceremonial purposes) to seek accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

The Joint Service Regulation also cites the National Institutes of Health (NIH) 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 that proper care and humane treatment are given to all animals used in research, testing, and education. This care requires scientific and professional judgment, which is based on knowledge of the husbandry needs of each species, as well as the special requirements of the research program.

AAALAC accreditation, widely accepted by the scientific community, is viewed as a highly 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. A copy of the AAALAC instructions for completing the description of the institutional animal care and use program as part of the application for AAALAC accreditation is provided as Appendix B. Accreditation covers all aspects of animal care to include: 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 non-biased, independent, external peer review which is fundamental to continuing AAALAC accreditation is valuable to any size program. AAALAC findings highlight program strengths and identify potential weaknesses. Laboratories

maintaining accreditation demonstrate a high degree of accountability and program excellence. AAALAC standards stress the appropriate appointment, composition, and empowerment of an Institutional Animal Care and Use Committee (IACUC). This Committee is responsible for monitoring and evaluating all aspects of the institution's program which use animals for teaching and/or research purposes. The scope of IACUC functions is addressed in Section V of this report.

DoD utilizes external peer review for the evaluation of many of its programs, such as drug screening laboratories, and review of military medical facilities by the Joint Commission for Accreditation of Health Organizations. At the same time, DoD recognizes the diversity of mission operations and global reach of the military mission. There are situations where external peer reviews are not cost effective due to the remote locale, limited scope of operations, or host nation sovereignty. In these cases, equivalency standards can apply and be effectively monitored. The Joint Service Regulation and Service-conducted inspections of facilities implement the requirements of the Animal Welfare Act and the *Guide for the Care and Use of Laboratory Animals*. As noted in the Office of the Inspector General, Department of Defense (OIG-DoD) "Review of the Use of Animals in DoD Medical Research Facilities," February 1994, best practices were found in both AAALAC and non-AAALAC accredited DoD facilities.

There are 51 DoD facilities that deal with animal use. Six of these are offices that control the extramural programs. Of the 45 DoD research, education, training and testing facilities, there are three instances where two facilities share a single animal care facility. Of the 42 separate animal facilities, 25 facilities or 60% are accredited by AAALAC (OIG-DoD, "Review of the Use of Animals in DoD Medical Research Facilities," February 1994). This compares favorably with the accreditation rate for the 1474 United States Department of Agriculture (USDA) registered animal facilities; 554 or 38% are accredited by AAALAC. Information on AAALAC accreditation by facility is given in Appendix C.

In keeping with the Joint Regulation, the DoD has accredited the majority of its research laboratories. However, as documented by the DoD Inspector General's report to Congress, a number of Department research facilities are dated in regards to their physical plant. These facilities have been historically regarded by the DoD as insurmountable obstacles to AAALAC accreditation until they are renovated or replaced. However, the AAALAC philosophy of accreditation is steadily evolving from a strictly physical facility perspective (engineering standards) to a more comprehensive evaluation of the total laboratory animal care and use program (performance standards). Facilities are still an important consideration in the accreditation process, but are no longer the paramount element. Consequently, research units that were previously regarded as unaccreditable until major facilities renovations or upgrades were completed, are now actively pursuing AAALAC accreditation on the basis of comprehensive, high quality laboratory animal care and use programs. However, there remain several DoD laboratories that require major construction or renovation prior to achieving full AAALAC accreditation. The lack of accreditation or deficiencies in the physical plant at several DoD facilities does not

imply that animals are exposed to unhealthy conditions. The OIG-DoD's report "Review of the Use of Animals in DoD Medical Research Facilities," February 1994 confirmed the effectiveness of animal husbandry programs in DoD facilities and concluded that although not all facilities were AAALAC accredited, animals in DoD facilities were maintained in healthy environments and treated humanely.

## SECTION III

# SERVICE AND DoD ANIMAL USE IN RESEARCH, EDUCATION, TRAINING AND TESTING, AND THE COST OF ANIMAL-BASED PROGRAMS VS. OTHER RESEARCH

---

---

This Section provides an in-depth report on Service and Department of Defense (DoD) animal use in research, education, training and testing.

### III.1. METHODS

Information was solicited and received from DoD agencies, military Commands and extramural sites involved in the performance and/or funding of animal care and use programs. DoD facilities included those located outside of the United States.

Animal was defined as any whole nonhuman vertebrate, living or dead, which 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 on hand in the facility or acquired during fiscal year (FY) 1993 were included. Animal organs, tissues, cells, blood, fluid components, and/or by-products purchased or acquired as such animal/biological components were not reported. This definition *does not* include animals used or intended for use as food for consumption by humans, animals used for ceremonial purposes, nor military working animals and their training programs.

DoD and service accounting systems do not contain resource subcategories to support provision of specific cost data for all direct and indirect costs associated with animal use programs. Each facility provided its own best estimate of these animal program costs.

### III.2. RESULTS

Information concerning total DoD utilization of animals by each Service is presented in figure III-1. DoD animal use by species is presented in figure III-2. The majority (94%) of animals used by the DoD consists of rodents, reptiles, amphibians and fish. Additional information on the types of species used by each service and the Tri-Service laboratories is presented in figures III-3 - III-6. Six categories of animal utilization were identified to include adjuncts to animal use research and/or alternatives to animal investigations, animal breeding stock, clinical investigations, medical research and development, non-medical research and development, and training and instruction. Figure III-7 illustrates that 75% of the animals used by the DoD for FY93 were in medical research. There was no use of DoD animals reported in FY93 for offensive weapon testing. Figures III-8 - III-11 provide additional information on animal use by category for each service and the Tri-Service laboratories. The total DoD species use by category is presented in figure III-12.

service and the Tri-Service laboratories. The total DoD species use by category is presented in figure III-12.

The costs of animal use programs relative to total research, education, training and testing programs are presented in tables III-1 through III-5. The tables provide data concerning Departmental research and development funding of animal use programs at each facility engaged in animal use programs. In addition, any non-DoD research and development funding received to support these programs has been indicated. Research and development funds are identified within the Department as Major Force Program 6, or P-6 funds. Training and education activities utilizing animals are supported with Major Force Program 8, or P-8 funds. These funds are also presented for those activities engaged in training and education. If non-DoD training and education funds are received for support of these latter programs, they are also displayed. Finally, the percentage of the total funds that are utilized by each facility for animal use programs is presented. There is considerable variation in this percentage which reflects the different missions performed in these facilities. Those facilities whose primary mission is medical research have higher percentages of animal use than laboratories that have a non-biological research mission.

Table III-5 is the DoD-wide total of animal use program dollars as compared to total program dollars. For RDT&E programs, those using animals accounted for 0.4% of the DoD-wide FY93 RDT&E budget.

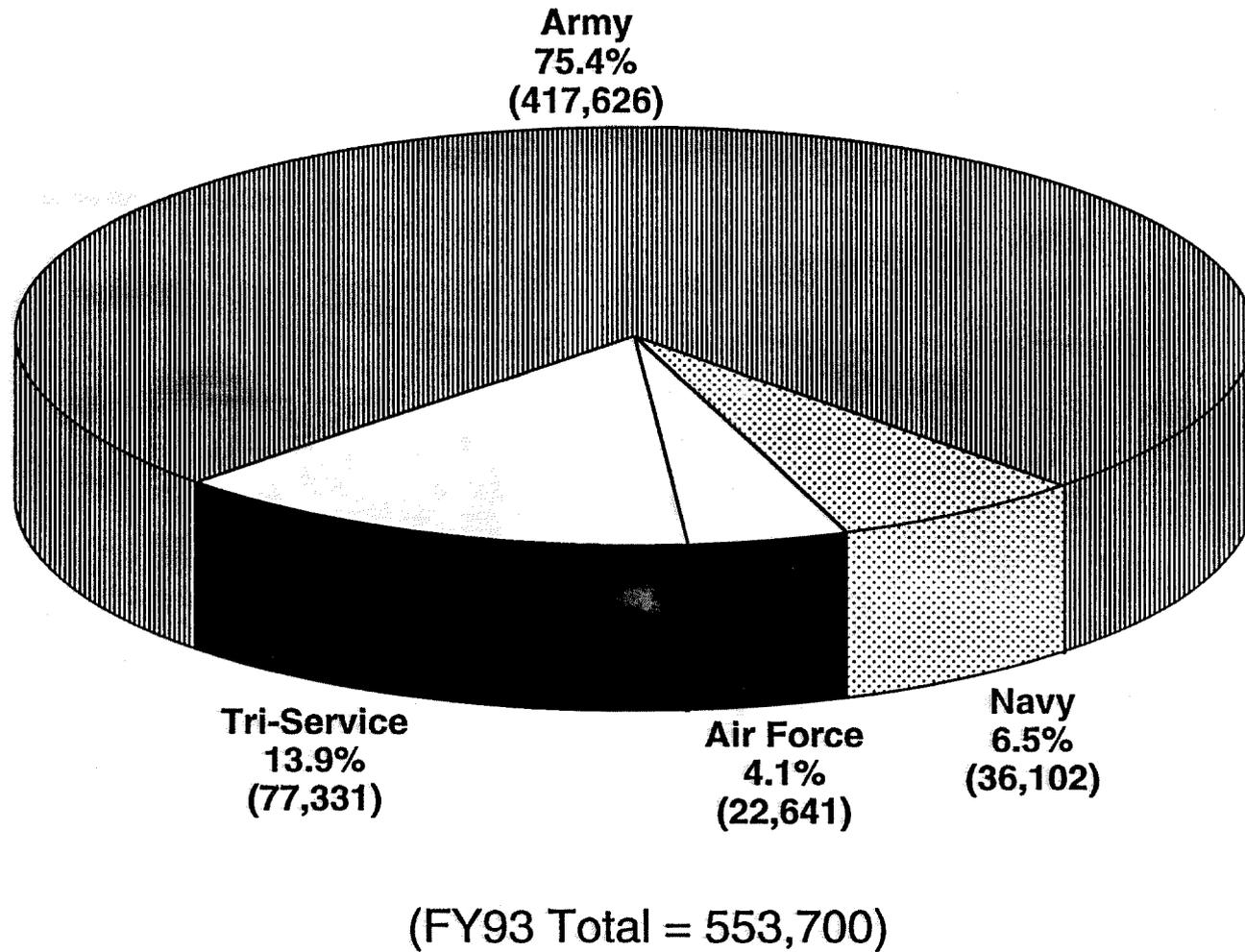
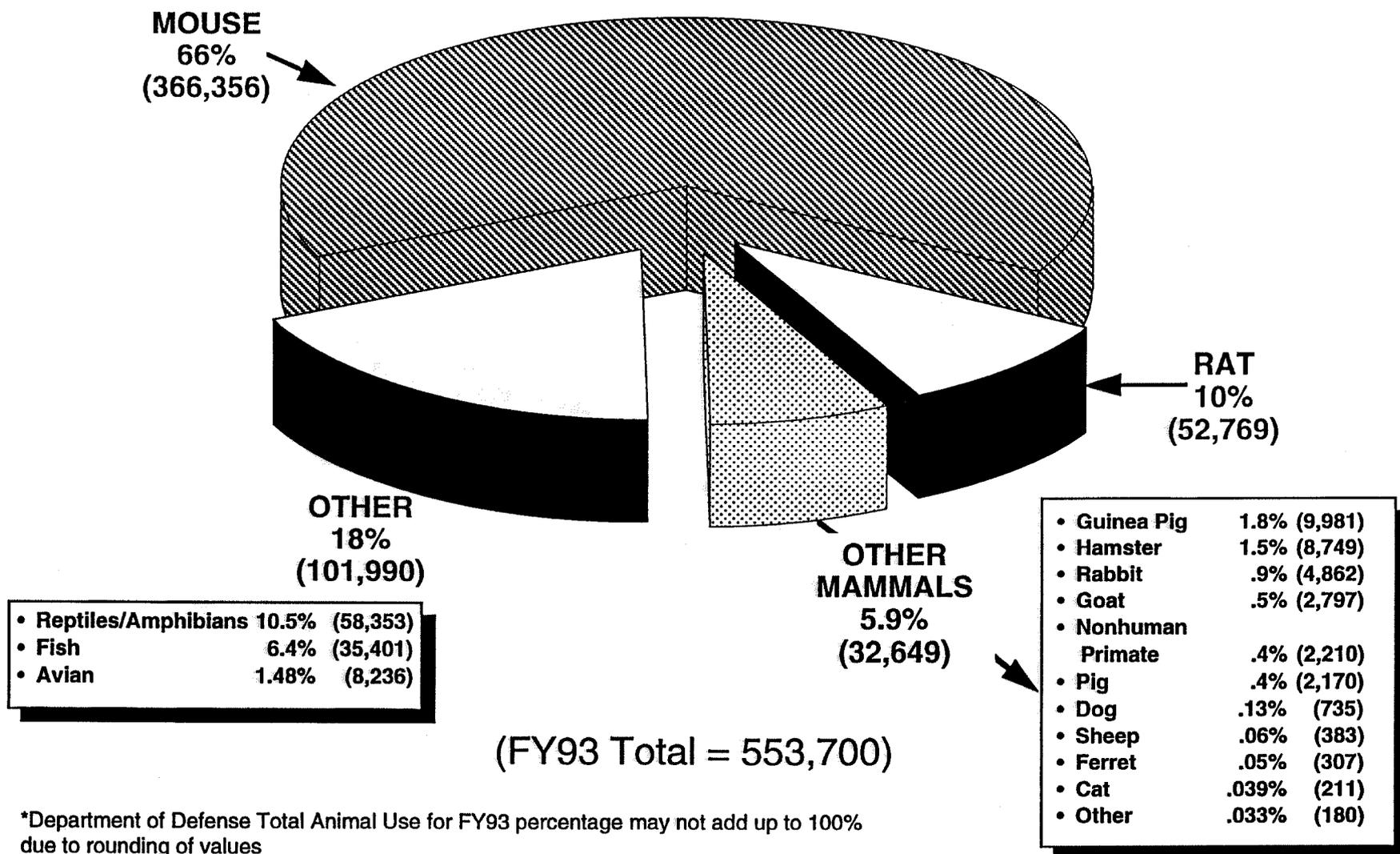


Figure III-1 Total DoD Intramural and Extramural Animal Use by Branch

III-4



\*Department of Defense Total Animal Use for FY93 percentage may not add up to 100% due to rounding of values

**Figure III-2 Total DoD Intramural and Extramural Animal Use by Species FY93**

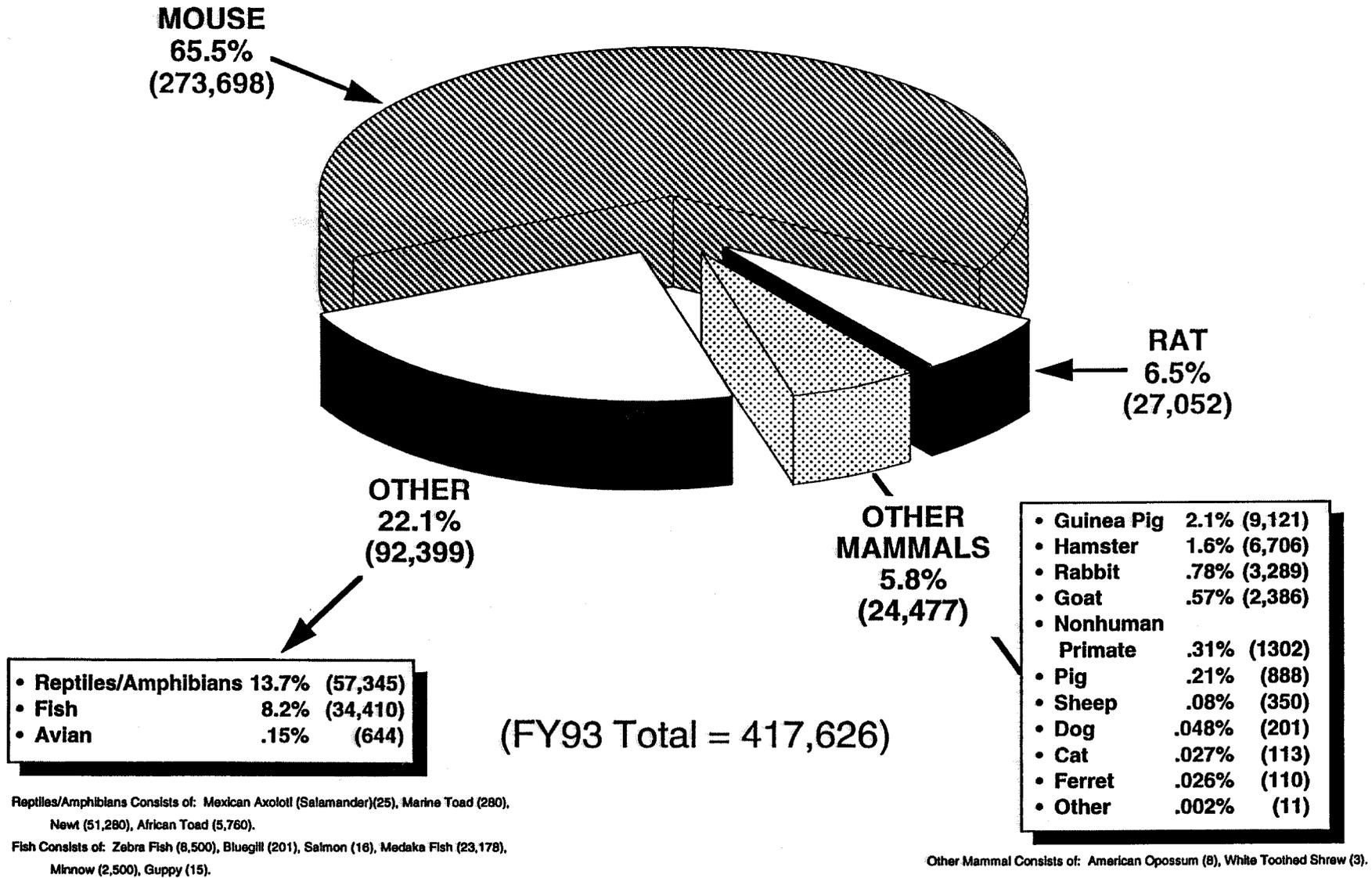
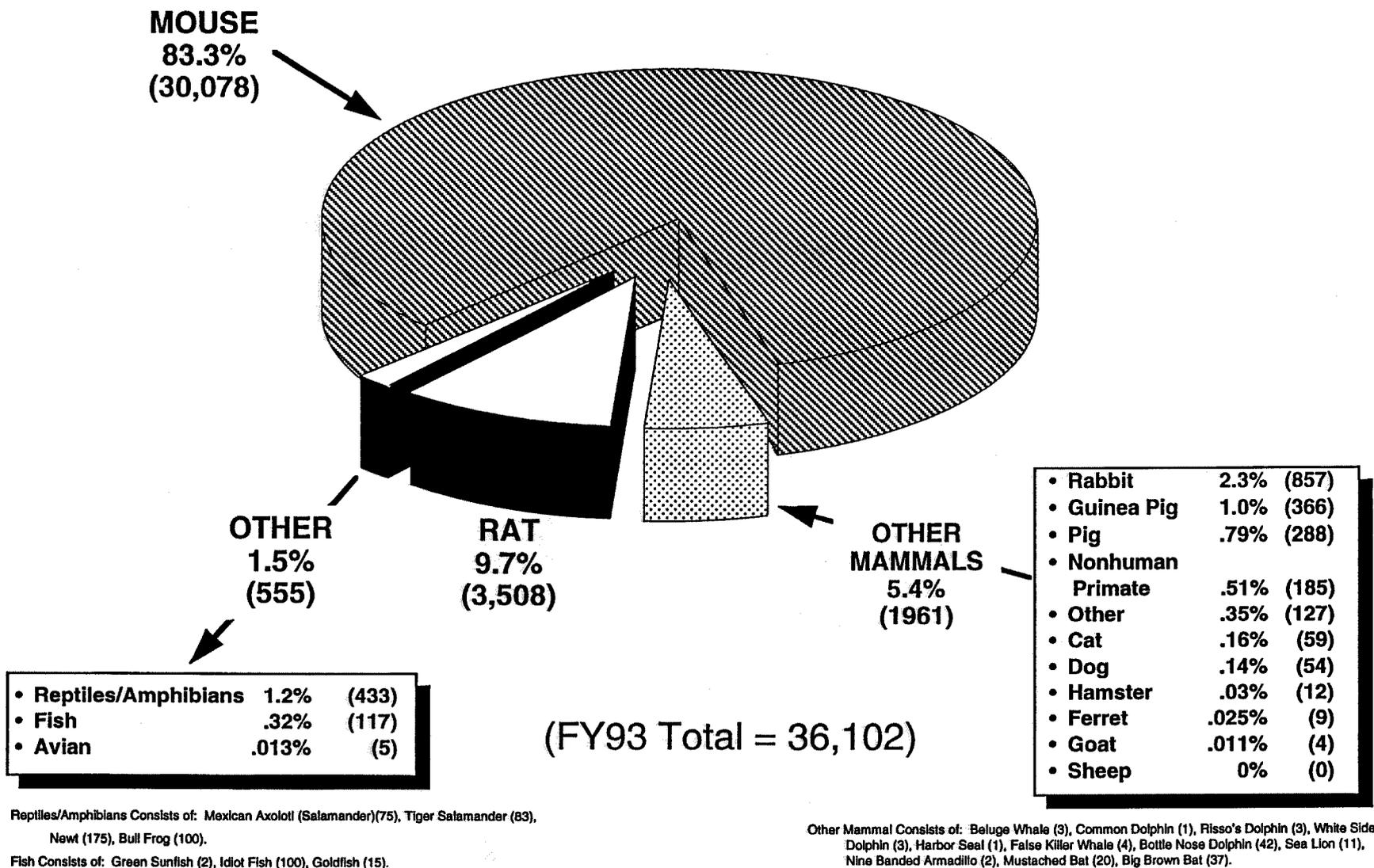


Figure III-3 Total Army Intramural and Extramural Animal Use by Species FY93

III-6



**Figure III-4 Total Navy Intramural and Extramural Animal Use by Species FY93**

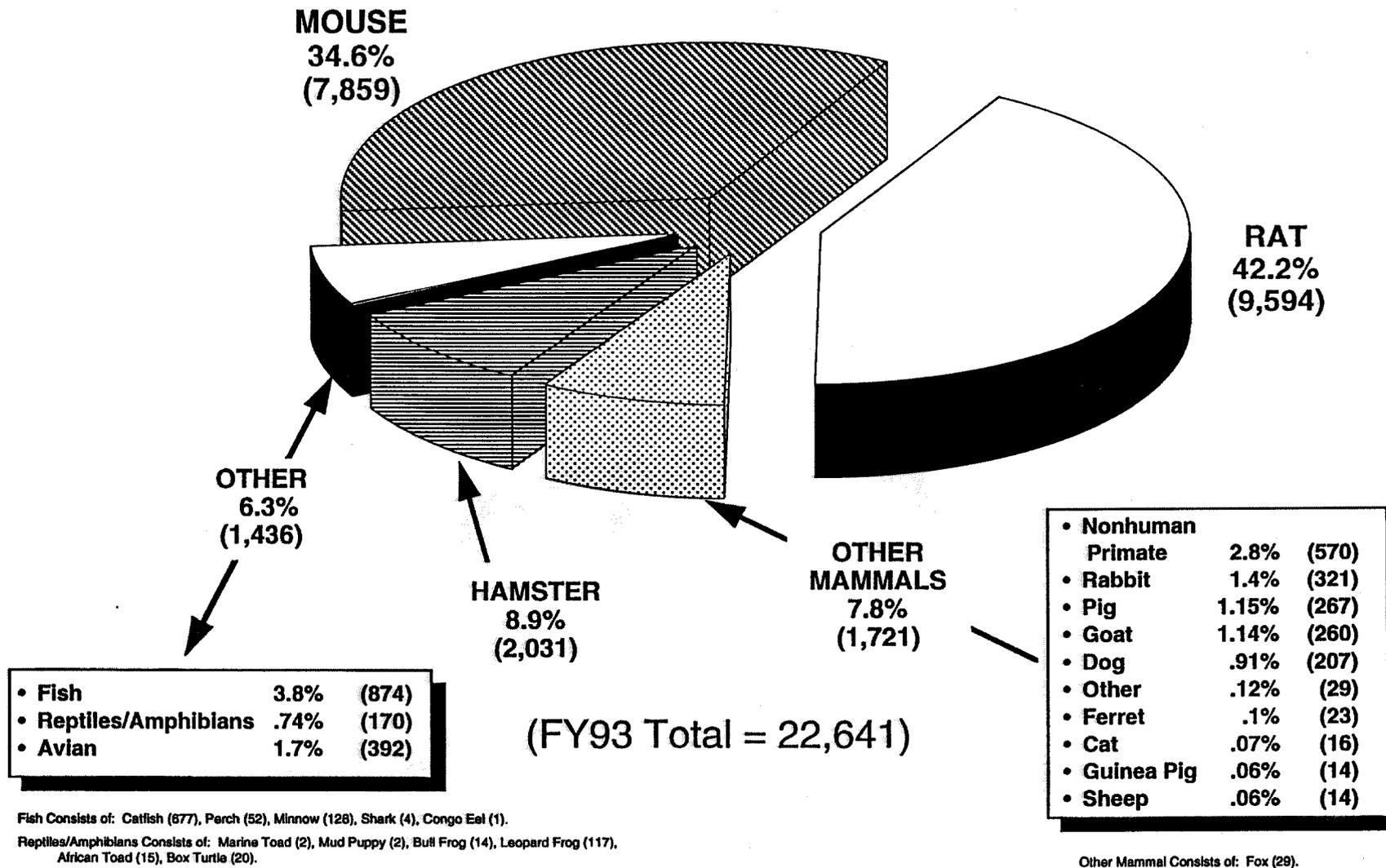
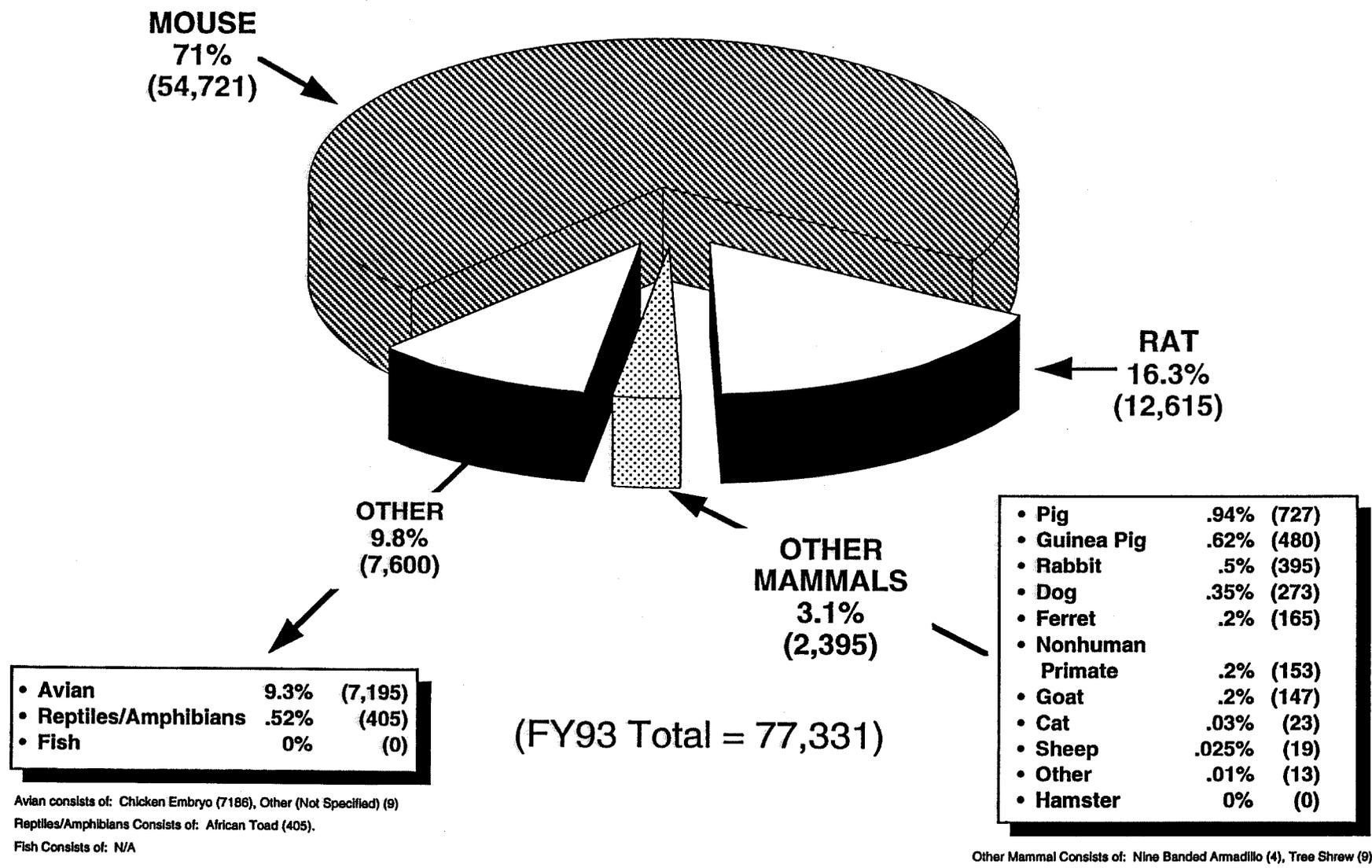
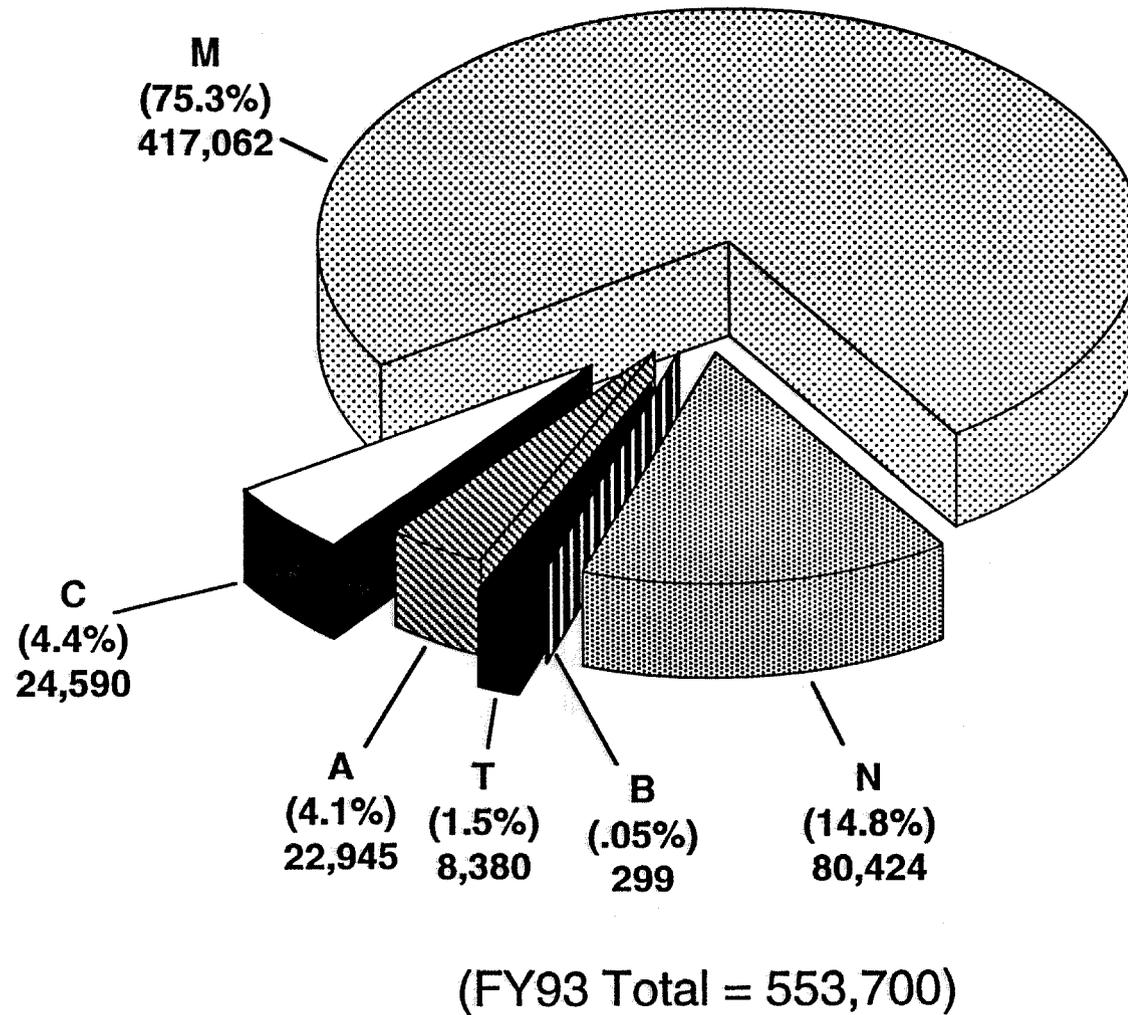


Figure III-5 Total Air Force Intramural and Extramural Animal Use by Species FY93

8-III



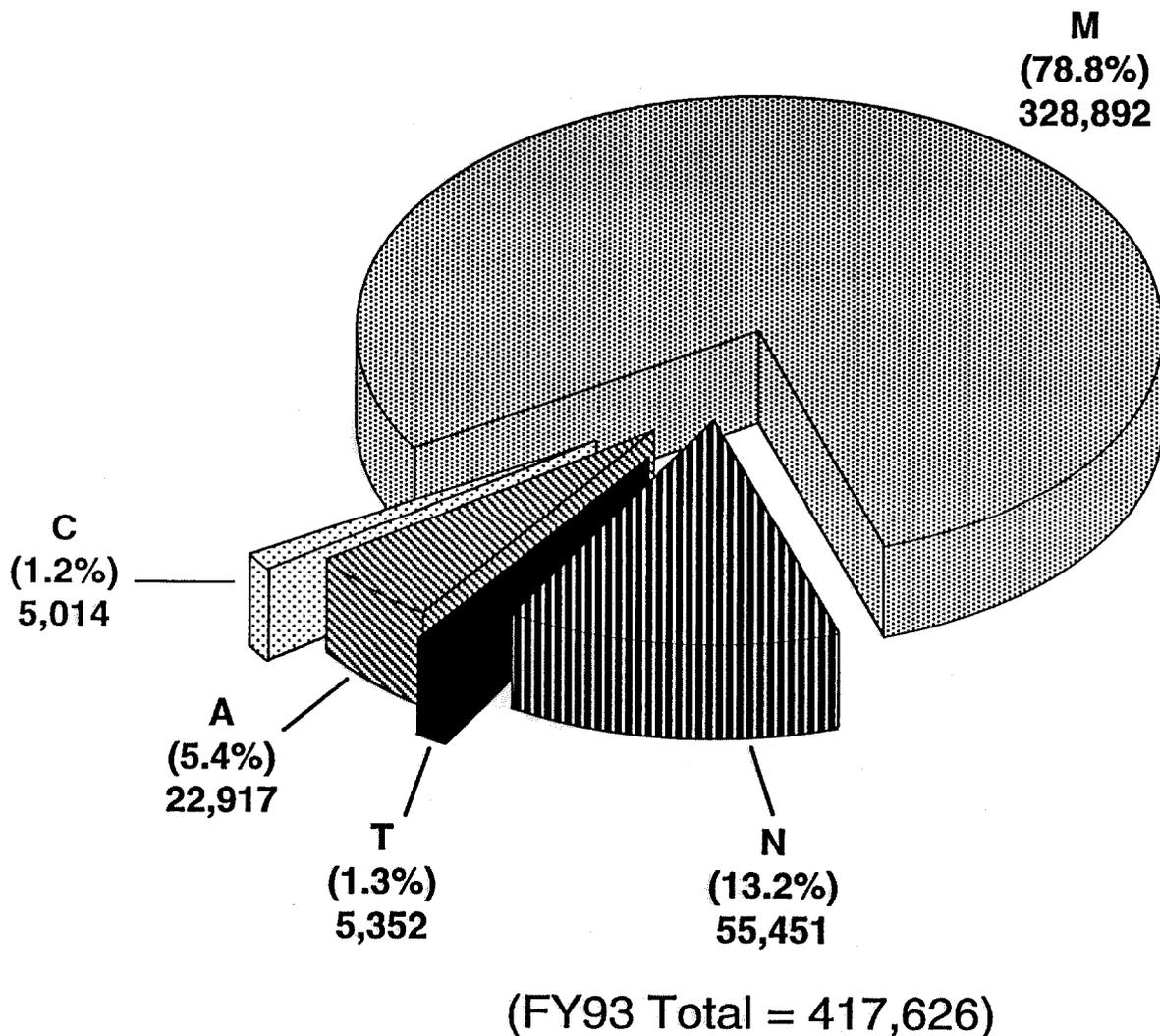
**Figure III-6 Total Tri-Service DoD Facility Intramural and Extramural Animal Use by Species FY93**



A: Adjuncts to Animal Use Research and/or Alternatives to Animal Investigation, B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E, N: Non-Medical RDT&E, T: Training & Instructional.

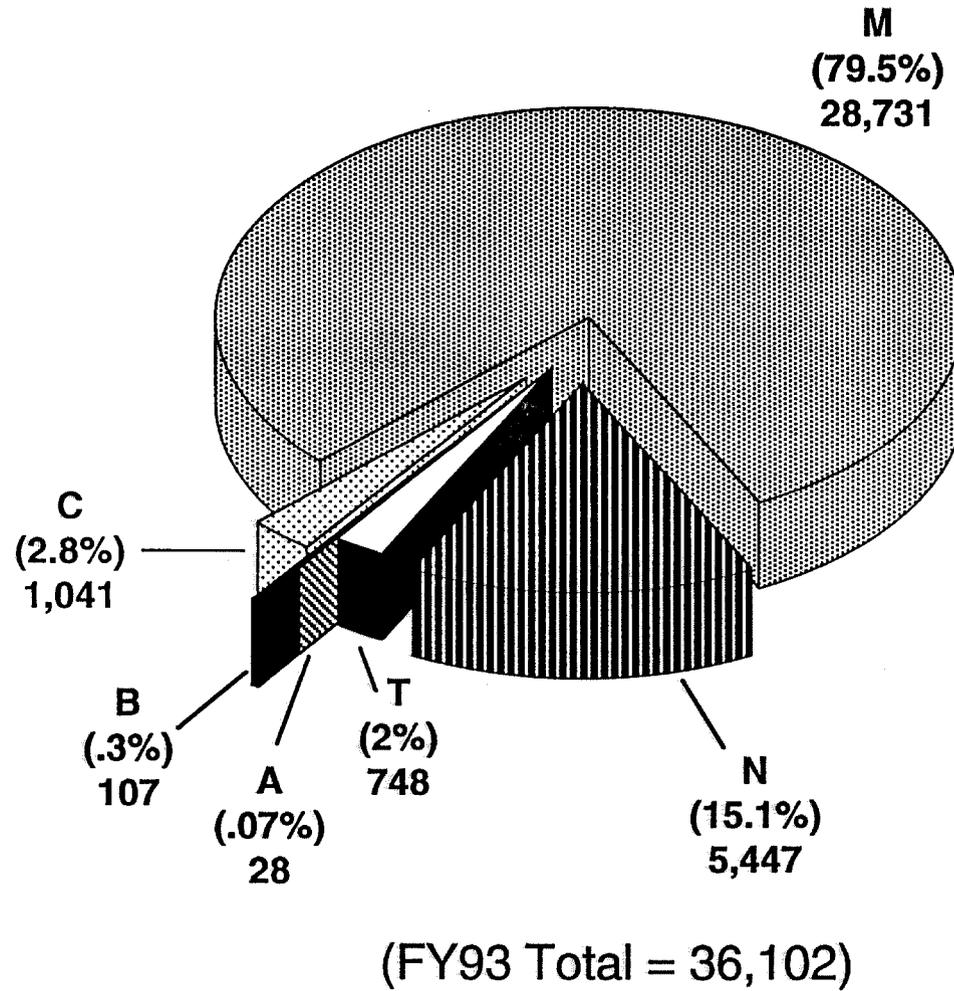
Figure III-7 Total DoD Intramural and Extramural Animal Use by Category

III-10



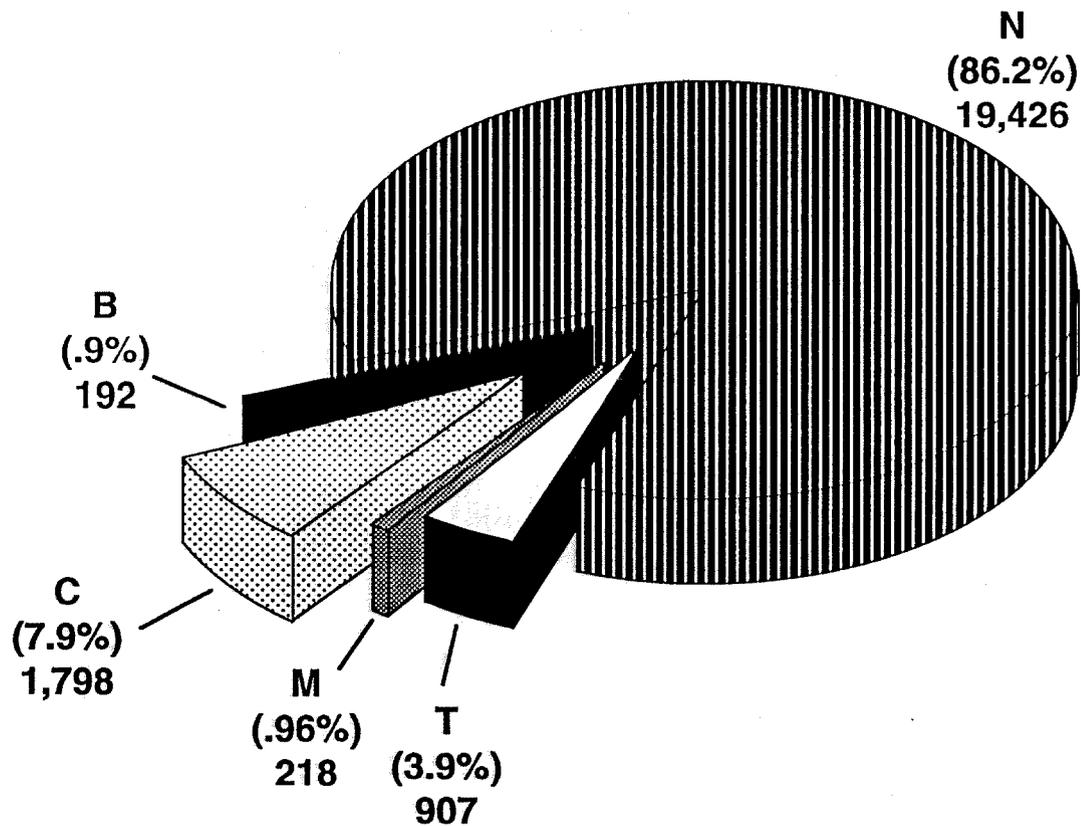
A: Adjuncts to Animal Use Research and/or Alternatives to Animal Investigation,  
C: Clinical Investigations, M: Medical RDT&E, N: Non-Medical RDT&E, T: Training & Instructional.

Figure III-8 Total Army Intramural and Extramural Animal Use by Category



A: Adjuncts to Animal Use Research and/or Alternatives to Animal Investigation,  
B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E,  
N: Non-Medical RDT&E, T: Training & Instructional.

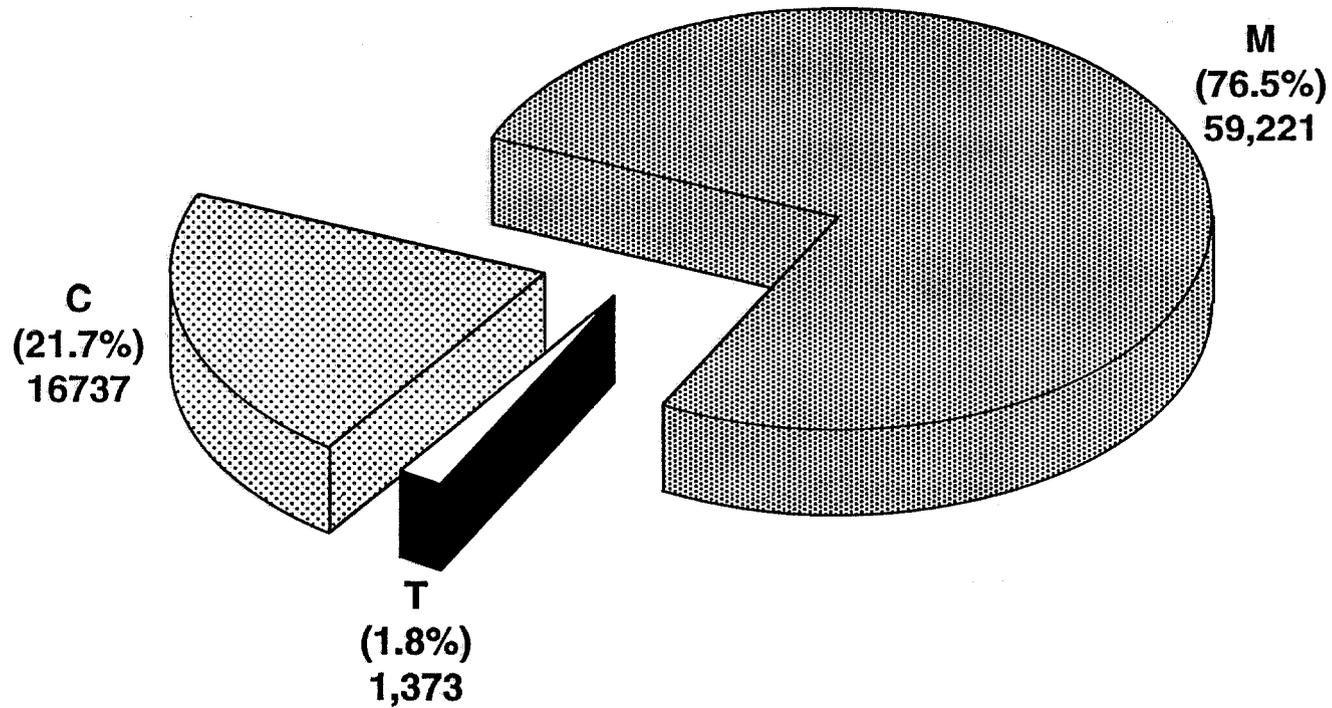
Figure III-9 Total Navy Intramural and Extramural Animal Use by Category



(FY93 Total = 22,641)

B: Animal Breeding Stock, C: Clinical Investigations, M: Medical RDT&E,  
N: Non-Medical RDT&E, T: Training & Instructional.

Figure III-10 Total Air Force Intramural and Extramural Animal Use by Category



(FY93 Total = 77,331)

C: Clinical Investigations, M: Medical RDT&E, T: Training & Instructional.

Figure III-11 Total Tri-Service DoD Facility Intramural and Extramural Animal Use by Category

III-14

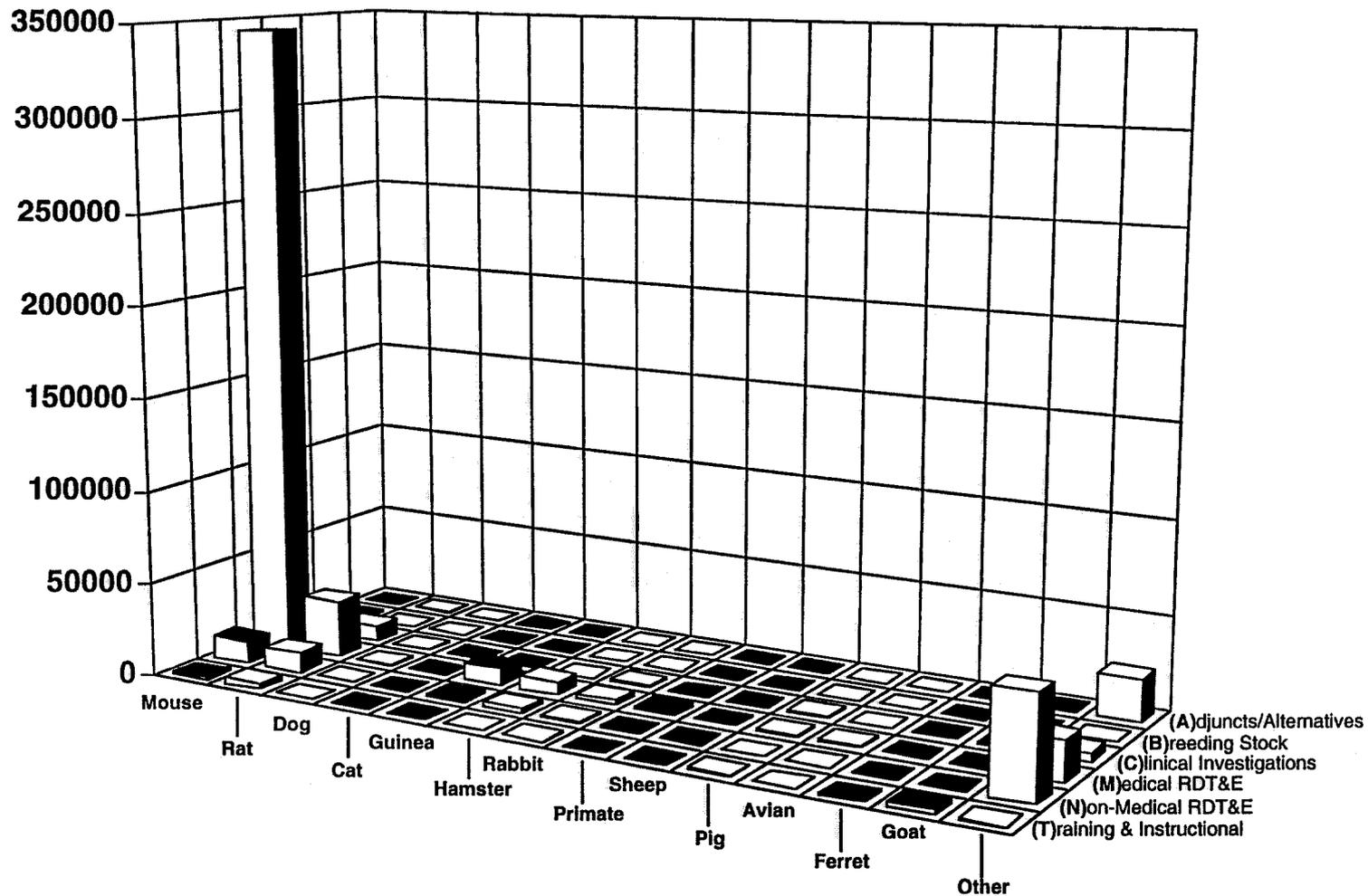


Figure III-12 Total DoD Intramural and Extramural Species Use by Category

**TABLE III-1 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - ARMY  
Research**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
U.S. Army Research Institute of Environmental Medicine	2,185	0	2,185	8,008	6	8,014	27
U.S. Army Medical Research Institute of Chemical Defense	6,563	0	6,563	19,514	24	19,538	34
U.S. Army Medical Research Institute of Infectious Diseases	12,882	0	12,882	27,391	0	27,391	47
U.S. Army Aeromedical Research Laboratory	559	0	559	7,764	0	7,764	7
U.S. Army Institute of Surgical Research	396	0	396	7,396	0	7,396	5
U.S. Army Biomedical Research and Development Laboratory	4,360	0	4,360	6,075	0	6,075	72
Walter Reed Army Institute of Research (WRAIR)	12,200	0	12,200	45,985	236	46,221	26
U.S. Army Medical Research Unit/3501, Brazil (WRAIR)	1	0	1	583	0	583	0.2
U.S. Army Medical Research Unit, Kenya (WRAIR)	31	0	31	288	0	288	11
Armed Forces Research Institute of Medical Sciences, Thailand (WRAIR)	366	11	397	5,943	655	6,598	6
U.S. Army Dental Research Detachment	871	0	871	2,461	0	2,461	35
U.S. Army Research Laboratory Human Research and Engineering	0	0	0	19,761	0	19,761	0
U.S. Army Edgewood Research, Development and Engineering Center (U.S. Army Chemical and Biological Defense Command)	1,208	0	1,208	161,499	0	161,499	1
Army Research Office, Research Triangle Park (Extramural Contracts)	281	0	281	77,433	0	77,433	0.4
Letterman Army Institute of Research (Closure Expense, Closed Effective Oct 93)	0	0	0	3,890	0	3,890	0
U.S. Army Medical Materiel Development Activity (Contract Monitoring)	0	0	0	4,836	5	4,841	0
U. S. Army Medical Research, Development, Acquisition and Logistics Command (Provisional) (Extramural Contracts)	58,563	0	58,563	144,175	410	144,585	41
<b>TOTALS</b>	<b>100,486</b>	<b>11</b>	<b>100,497</b>	<b>543,002</b>	<b>1,336</b>	<b>544,338</b>	<b>18</b>

III-15

DOD Animal Cost and Use Programs 1993

**TABLE III-1 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - ARMY (Continued)  
Education**

<b>Institution (Column A)</b>	<b>DOD Funding Animal Use Programs (K\$) (Column B)</b>	<b>Non-DOD Funding Animal Use Programs (K\$) (Column C)</b>	<b>Total Funding Animal Use Programs (K\$) (Column B+C=D)</b>	<b>DOD Funding Total Program RDT&amp;E or Training (K\$) (Column E)</b>	<b>Non-DOD Funding Total Program (K\$) (Column F)</b>	<b>Total Program Costs (K\$) (Column E+F=G)</b>	<b>% of Program Costs In Animal Use Programs (Column D/G=H)</b>
Walter Reed Army Medical Center	483	28	509	3,768	735	4,503	11
William Beaumont Army Medical Center	79	0	79	1,235	478	1,713	5
Tripler Army Medical Center	223	174	397	687	174	861	46
Fitzsimons Army Medical Center	226	0	226	1,823	185	2,008	11
Madigan Army Medical Center	20	122	142	476	279	755	19
Dwight David Eisenhower Army Medical Center	248	0	248	675	0	675	37
Brooke Army Medical Center	44	0	44	805	125	930	5
<b>TOTALS</b>	<b>1,323</b>	<b>322</b>	<b>1,645</b>	<b>9,469</b>	<b>1,976</b>	<b>11,445</b>	<b>14</b>

III-16

**TABLE III-1 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - ARMY (Continued)  
Training**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Army Medical Department Center & School	54	0	54	12,300	0	12,300	0.4
Special Warfare Training Group	255	0	255	857	0	857	30
<b>TOTALS</b>	<b>309</b>	<b>0</b>	<b>309</b>	<b>13,157</b>	<b>0</b>	<b>13,157</b>	<b>2</b>

**Testing**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
U.S. Army Dugway Proving Ground	775	0	775	53,964	289	54,253	1
Army Environmental Hygiene Agency	704	0	704	28,402	0	28,402	2
<b>TOTALS</b>	<b>1,479</b>	<b>0</b>	<b>1,479</b>	<b>82,366</b>	<b>289</b>	<b>82,655</b>	<b>2</b>

III-17

DOD Animal Cost and Use Programs 1993

**TABLE III-1 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - ARMY (Continued)  
Summary**

III-18

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
Army Research in Facilities with Animal Use Programs	100,486	11	100,497	543,002	1,336	544,338	18
Army Testing in Facilities with Animal Use Programs	1,479	0	1,479	82,366	289	82,655	2
Total Army RDT&E*	101,965	11	101,976	6,057,072	1,625	6,058,697	2
Army Education in Facilities with Animal Use Programs	1,323	322	1,645	9,489	1,976	11,445	14
Army Training in Facilities with Animal Use Programs	309	0	309	13,157	0	13,157	2

\* RDT&E Programs (R-1), Department of Defense Budget for Fiscal Year 1995, February 1994

**TABLE III-2 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - NAVY  
Research**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
Naval Aerospace Medical Research Laboratory	684	0	684	5,383	16	5,399	13
Naval Dental Research Institute	630	0	630	1,619	0	1,619	39
Naval Medical Research Institute	9,355	0	9,355	55,298	114	55,412	17
U.S. Naval Medical Research Unit #2, Indonesia	81	0	81	4,118	0	4,118	2
U.S. Naval Medical Research Unit #3, Cairo Egypt	1,180	630	1,810	6,871	720	7,591	24
U.S. Naval Medical Research Institute Detachment #3800, Peru	401	0	401	1,956	0	1,956	21
Naval Medical Research Institute Toxicology Division	1,432	0	1,432	3,019	0	3,019	47
Naval Command, Control & Ocean Surveillance Center RDTE	4,600	0	4,600	328,988	0	328,988	1
Office of Naval Research (Extramural Contracts)	6,937	0	6,937	31,148	0	31,148	22
Naval Medical Research and Development Command (Extramural Contracts)	4,514	0	4,514	36,027	0	36,027	13
<b>TOTALS</b>	<b>29,814</b>	<b>630</b>	<b>30,444</b>	<b>474,427</b>	<b>850</b>	<b>475,277</b>	<b>6</b>

**Education**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
Naval Medical Center, Clinical Investigation Program, Oakland, CA	38	0	38	120	0	120	32
Naval Medical Center, Clinical Investigation Program, San Diego, CA	517	0	517	601	0	601	86
Naval Medical Center, Clinical Investigation Program, Portsmouth, VA	121	0	121	427	0	427	28
<b>TOTALS</b>	<b>676</b>	<b>0</b>	<b>676</b>	<b>1,148</b>	<b>0</b>	<b>1,148</b>	<b>59</b>

III-19

DOD Animal Cost and Use Programs 1993

**TABLE III-2 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - NAVY (Continued)  
Summary**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Navy Research in Facilities with Animal Use Programs	29,814	630	30,444	474,427	850	475,277	6
Navy Testing in Facilities with Animal Use Programs	0	0	0	0	0	0	0
<b>Total Navy RDT&amp;E*</b>	<b>29,814</b>	<b>630</b>	<b>30,444</b>	<b>8,857,441</b>	<b>850</b>	<b>8,858,291</b>	<b>0.3</b>
Navy Education in Facilities with Animal Use Programs	676	0	676	1,148	0	1,148	59
Navy Training in Facilities with Animal Use Programs	0	0	0	0	0	0	0

\* RDT&E Programs (R-1), Department of Defense Budget for Fiscal Year 1995, February 1994

**TABLE III-3 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS - AIR FORCE  
Research**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Armstrong Laboratory, Wright Patterson AFB/ Brooks AFB	10,500	273	10,773	192,558	914	193,472	6
Aerophysics Systems Flight Office	164	0	164	7,121	0	7,121	2
Air Force Office of Scientific Research (Extramural Contracts)	4,200	0	4,200	202,000	0	202,000	2
<b>TOTALS</b>	<b>14,864</b>	<b>273</b>	<b>15,137</b>	<b>401,679</b>	<b>914</b>	<b>402,593</b>	<b>4</b>

**Education**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Keesler Medical Center, 81st Medical Group	80	2	82	492	42	534	15
Wilford Hall Medical Center	1,174	44	1,218	3,470	901	4,371	28
David Grant USAF Medical Center 60th Med Group	182	21	203	322	280	602	34
U.S. Air Force Academy	3	0	3	92	0	92	3
<b>TOTALS</b>	<b>1,439</b>	<b>67</b>	<b>1,506</b>	<b>4,376</b>	<b>1,223</b>	<b>5,599</b>	<b>27</b>

III-21

DOD Animal Cost and Use Programs 1993

**TABLE III-3 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS -AIR FORCE (Continued)  
Summary**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
Air Force Research in Facilities with Animal Use Programs	14,864	273	15,137	401,679	914	402,593	4
Air Force Testing in Facilities with Animal Use Programs	0	0	0	0	0	0	0
Total Air Force RDT&E*	14,864	273	15,137	12,866,924	914	12,867,838	0.1
Air Force Education in Facilities with Animal Use Programs	1,439	67	1,506	4,376	1,223	5,599	27
Air Force Training in Facilities with Animal Use Programs	0	0	0	0	0	0	0

\* RDT&E Programs (R-1), Department of Defense Budget for Fiscal Year 1995, February 1994

**TABLE III-4 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS  
TRI-SERVICE DOD FACILITIES  
Research**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Armed Forces Institute of Pathology	820	288	1,108	29,247	720	29,967	4
Armed Forces Radiobiology Research Institute	15,082	318	15,380	17,292	318	17,610	87
<b>TOTALS</b>	<b>15,882</b>	<b>606</b>	<b>16,488</b>	<b>46,539</b>	<b>1,038</b>	<b>47,577</b>	<b>35</b>

**Education**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs In Animal Use Programs (Column D/G=H)
Uniformed Services University of the Health Sciences	5,905	11,172	17,077	53,499	16,256	69,755	24
<b>TOTALS</b>	<b>5,905</b>	<b>11,172</b>	<b>17,077</b>	<b>53,499</b>	<b>16,256</b>	<b>69,755</b>	<b>24</b>

III-23

DoD Animal Cost and Use Programs 1993

**TABLE III-4 COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS  
TRI-SERVICE DOD FACILITIES (Continued)  
Summary**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
Research in Tri-Service Facilities with Animal Use Programs	15,882	606	16,488	46,539	1,038	47,577	35
Testing in Tri-Service Facilities with Animal Use Programs	0	0	0	0	0	0	0
Total Tri-Service Defense Agency RDT&E*	15,882	606	16,488	9,764,807	1,038	9,765,845	0.2
Education in Tri-Service Facilities with Animal Use Programs	5,905	11,172	17,077	53,499	16,256	69,755	24
Training in Tri-Service Facilities with Animal Use Programs	0	0	0	0	0	0	0

\*RDT&E Programs (R-1), Department of Defense Budget for Fiscal Year 1995, February 1994

**TABLE III-5 DOD COSTS OF ANIMAL USE PROGRAMS RELATIVE TO  
TOTAL RESEARCH, EDUCATION, TRAINING, AND TESTING PROGRAMS  
Summary**

Institution (Column A)	DOD Funding Animal Use Programs (K\$) (Column B)	Non-DOD Funding Animal Use Programs (K\$) (Column C)	Total Funding Animal Use Programs (K\$) (Column B+C=D)	DOD Funding Total Program RDT&E or Training (K\$) (Column E)	Non-DOD Funding Total Program (K\$) (Column F)	Total Program Costs (K\$) (Column E+F=G)	% of Program Costs in Animal Use Programs (Column D/G=H)
DoD Research in Facilities with Animal Use Programs	161,046	1,520	162,566	1,465,647	4,138	1,469,785	11
DoD Testing in Facilities with Animal Use Programs	1,479	0	1,479	82,366	289	82,655	2
Total DoD RDT&E*	162,525	1,520	164,045	37,827,598	4,427	37,832,025	0.4
DoD Education in Facilities with Animal Use Programs	9,343	11,561	20,904	68,492	19,455	87,947	24
DoD Training in Facilities with Animal Use Programs	309	0	309	13,157	0	13,157	2

\* RDT&E Programs (R-1), Department of Defense Budget for Fiscal Year 1995, February 1994

## SECTION IV

# DEFENSE DEPARTMENT INITIATIVES TO PROMOTE ALTERNATIVE METHODS THAT REPLACE, REDUCE AND REFINE THE USE OF ANIMALS

This section responds to the Committee's direction that the Secretary of Defense describe initiatives to promote alternative approaches that bring about a reduction in animal usage. 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.

Department policy with regard to animal alternatives is promulgated in DoD Directive 3216.1 which indicates 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.

Retrospective data on DoD animal use during 1987, 1989 & 1991 (Weichbrod, 1993) were compared to an analogous subset of 1993 data. This subset was restricted to United States Department of Agriculture reportable species and rodents used at intramural sites in the Continental United States. These data demonstrate the Department's aggressive and effective application of these *Four Rs* and are reflected in a 40% (figure IV-1) decrease of intramural animal use in research over the past seven years.

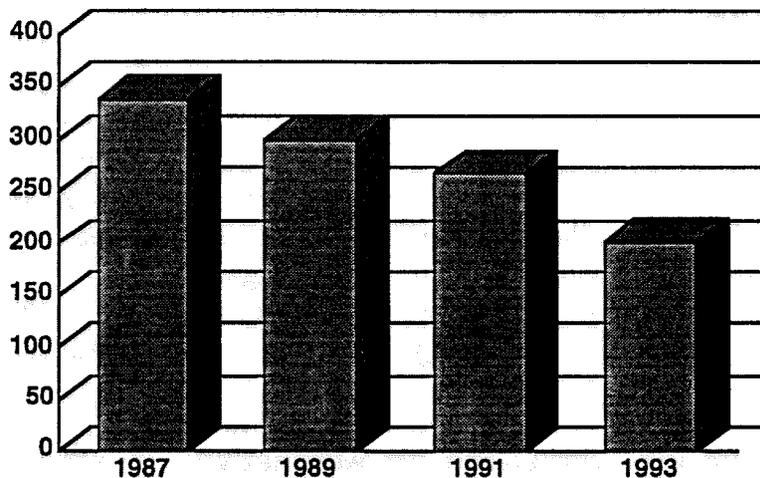


Figure IV-1 DoD Intramural Total Animal Use FY87-93

To illustrate the Department's initiatives to promote these *Four Rs*, this section provides a description of such initiatives within DoD's research laboratories and medical treatment centers. The following list is not all inclusive, as the number of specific examples of implementing alternative methods that can be documented for DoD's research projects is large. Rather, it illustrates the scope, diversity, and spirit of DoD's *Four Rs* initiatives. This section will demonstrate a broad-based movement, where feasible, towards the use of biotechnology and other innovative alternatives to replace and reduce animal use as well as refinement in methods used in essential animal studies.

#### **IV.1. RESPONSIBILITY**

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 towards implementing the *Four Rs* approach to minimizing animal use.

##### **IV.1.1 Science and Technology Emphasis on Alternatives to Animal Subjects of Research**

An example of the Department's direction on seeking alternatives to animal use is the fiscal year (FY) 1993 Army Science and Technology Objective (STO) entitled, *Reducing Reliance on Human and Animal Subjects of Research*. The specific task to "Develop refinement, reduction and replacement strategies for projects currently reliant on the use of animals" supports this STO and is designed to provide a positive mechanism for researchers to explore and implement alternatives to the use of animals. This provides both the impetus for alternatives implementation, as well as a mechanism for funding such research. In FY94, this Army STO was revised and strengthened. The title for this objective for FY94 is *Reducing Reliance on Animals for Research and Improving Experimental Conditions Using Animals* (ASTMP, FY 1994). The U.S. Army Medical Research, Development, Acquisition, and Logistics Command (Provisional) (USAMRDALC) budgets \$600,000 per year for this objective, which is available to support alternatives to animal use research in all three services.

Army STOs provide guidance, means, and high visibility to major Army technology initiatives. The Department of the Army, in coordination with the Director of Defense Research and Engineering (DDR&E), Office of the Secretary of Defense (OSD), publishes the *Army Science and Technology Master Plan* (ASTMP) as guidance to Army laboratories and research, development and engineering centers and to non-Army organizations supporting the Army science and technology (S&T) base.

##### **IV.1.2 Conferences and Workshops on Alternatives to Animal Use**

The DoD promotes responsibility for alternatives to animal use by augmenting formal education and training programs, and sponsors major meetings and

conferences on the subject. In 1990, an important conference on alternatives to animal use, "DoD Initiatives in Alternatives to Animal Testing," was held at Aberdeen Proving Ground. This was followed by a three-day symposium in 1992 entitled "Current Concepts and Approaches on Animal Test Alternatives" with 35 scientific platform sessions and 22 scientific poster presentations. This international symposium was attended by nearly 300 military and civilian scientists from four countries. The symposium was praised as a success by Dr. Martin Stephens of the Humane Society of the United States (Appendix D). Proceedings of the 1992 symposium were published in September 1993 and are available through the Defense Technical Information Center. The Department's continuing commitment to promoting responsibility for alternatives to animal use, even in an environment of constrained resources, is reflected by scheduling another such conference on 24-27 May 1994.

#### **IV.1.3 National Research Council, Institute of Laboratory Animal Resources (ILAR), 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 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 military-specific research. The Department funded a five-year ILAR grant (DAMD17-87-G-7021) for this program and has renegotiated a five-year extension to this effort committing diminishing research funds to maintain this important collaboration. Annual funding for this DoD-sponsored ILAR program is in excess of \$100,000.

#### **IV.1.4 Institutional Animal Care and Use Committee (IACUC) 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 IACUCs at its biomedical research facilities. Accordingly, DoD IACUCs consider alternatives to the proposed use of animals as an important review consideration.

#### **IV.1.5 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 addition to being advisors to the 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.

An important aspect of their responsibility is to review extramural animal use protocols, insuring that alternatives to animal use and personnel training issues have been addressed. The solicitation of extramural efforts through the Broad Agency Announcement (BAA) is very specific in requiring all applications using animals to address the question of alternatives. The following statement is included in the BAA.

"It is USAMRDALC policy that alternatives to the use of animal models be thoroughly investigated prior to submission of any protocol involving research animals. Offerers are required to identify the services that were used to obtain information on alternatives in this research. The USAMRDALC reserves the right to request evidence that an alternative search was performed."

These extramural applications are reviewed by military veterinary staff.

#### **IV.1.6 Professional Veterinary Training in LAM**

The presence of specialty trained, veterinary, LAM expertise in biomedical research institutions 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 President-elect and several past presidents of the American College of Laboratory Animal Medicine, several past presidents of the American Association of Laboratory Animal Science (AALAS), and current Secretary-Treasurer of the American Society of Laboratory Animal Practitioners. This traditional DoD strength in LAM expertise strongly enhances both animal care and use and animal alternatives programs.

#### **IV.1.7 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 Library explain in detail the resources available for exploring various animal alternatives in the laboratory. The Walter Reed Army Institute of Research (WRAIR) sponsors laboratory animal workshops that provide comprehensive technical training on animal use and related issues. Improving the technical expertise of laboratory animal technicians and investigators is

a significant refinement element for the use of animals in the laboratory. These workshops are available to all DoD and National Institutes of Health laboratories. As an example, the workshop on the use of rodents is offered 14 times per year. In addition, 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.

## **IV.2. DOD INITIATIVES TO REPLACE, REDUCE AND REFINER THE USE OF ANIMALS**

The following specific examples are a representative listing of alternatives methodologies practiced in DoD facilities. They are categorized as Replacement, Reduction, and Refinement initiatives. Because of the multi-faceted aspects of many of these examples, some logically belong in more than one category.

### **IV.2.1 Replacement**

The replacement alternative addresses supplanting animal use with non-living 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 45 United States Code, Section 46, "Protection of Human Subjects".

#### ***IV.2.1.A Replacement using biochemical or physical methods***

- Membrane feeding systems have been developed that replace the need to feed some types of blood-feeding flies and mosquitos on rodent hosts.

- Development of Polymerase Chain Reaction and Mammalian Cell Selection Assays for short-term genetic toxicity testing replaces animal use in carcinogenesis and mutagenesis studies.

- Efforts are ongoing to develop a polymerase chain reaction assay for Q fever that could eliminate the need for the use of a mouse bioassay.

- Quantitating bacterial endotoxin with an *in vitro*, Limulus Amebocyte test is used to replace *in vivo* pyrogen testing in rabbits.

- Use of predictive anthropomorphic dummies and manikins, eg. ADAM (ejection seat reactive live load manikin) and AIRMAN (a fragment capture live fire manikin) has replaced the use of animals in these studies.

#### ***IV.2.1.B Replacement using computer simulations***

- Computer models to replace rhesus monkeys and baboons for toxicological studies are being developed.

- Development of computational models of dolphin echolocation (sonar) for inclusion in the development of hardware systems will replace use of animals as object detectors.

- Development for Special Forces (SF) medical training personnel of advanced computer technology using Virtual Reality, Holographic Imaging, and Telepresence Surgery techniques should replace the use of animals in SF surgical training.

- Computer models are being developed for predicting carcinogenesis induced by ionizing radiation replacing the need to use animals.

#### ***IV.2.1.C Replacement using in vitro cell culture***

- *In vitro* cell culture methods have been developed for passage of Hepatitis E virus eliminating use of animals for virus propagation.

- Development of a macrophage cell line to replace animals in evaluation of cytotoxicity and genotoxicity of respirable particles is in progress.

- Development of a fish liver cell culture model for evaluating metabolism of Xenobiotic compounds replaces the use of mammalian animal models.

- Study of the effects of growth factors on human fibroblasts is being conducted in cell culture media replacing the dogs and pigs utilized in previous studies.

- Development of a cell culture system to pass human breast cancer cells eliminates the need for initially passing these cells in a nude mouse model.

- Use of immortalized tissue culture systems or isolated lobster neuronal cells to investigate radiation effects and free radical damage to the nervous system at the molecular level are used to replace similar protocols using rats and guinea pigs.

- Wound-healing studies on space shuttle flights STS-45, 55 and 56 used a cell culture flight module instead of live rats.

- Development of human skin cell and animal processing plant skin models for assessing cellular mediator and tissue damage from environmental heat has replaced mammalian laboratory animal use.

#### ***IV.2.1.D Replacement with non-mammalian species***

- Development of an aquatic bioassay using the medaka fish (*Oryzias latipes*) to assess human carcinogenic health risks replaces laboratory animal use for tumor immunodiagnosis.

**IV.2.1.E Replacement with human tissue, or volunteers as protocols progress to human trials**

- Many procedures including conjunctival impression cytology, salt and water balance and intestinal permeability, neuroendocrine assessment, nutritional support, testing of topical treatments and studies of *in vitro* activated keratinocytes in autografts in thermal injury research were previously performed in animals but have now progressed to human use protocols, eliminating the use of animals.

- Biomechanical analysis of the strength of plate fixation devices for long bone fracture repair is being performed with human cadaver bones and metal substitutes thereby replacing animal studies.

**IV.2.1.F Replacement with discarded tissue from other laboratories or food processing plants**

- Pigs feet obtained from a local plant are used for teaching surgical suturing procedures, which replaces the need for use of live animals.

- Sheep parts purchased from a processing plant are used to train dentists on periodontal surgical procedures replacing the use of live animals for training.

- Ocular researchers are using eyes purchased from local cattle processing plants for studies instead of live rabbits.

**IV.2.2 Reduction**

Decreasing the numbers 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.

**IV.2.2.A Reduction by use of alternative screening methods to study efficacy in biological testing**

- Development of a Quantitative Luminescence Imaging System (QLIS) for screening radiofrequency radiation (RFR) biological effects in cells reduces the number of laboratory animals needed.

- Establishment of a tissue culture system to evaluate initial exposure levels of toxic substances, such as ammonia, or nitrogen and sulfur oxides, in lung and throat secretions reduces the use of animals in subsequent therapy studies.

- Development of an *in vitro* test using human peripheral blood could determine the effectiveness of toxoid in a staphylococcus enterotoxin B (SEB) vaccine and measure the effectiveness of potential treatments to SEB poisoning. If validated, this would significantly reduce the animals used in SEB research.

- Use of bacteria, algae, crustaceans, earthworms, flatworms, and a toxicity estimation software program functions as a screening mechanism in toxicity testing, highlighting those chemicals or materials necessitating further testing with fish or higher vertebrates. This eliminates many compounds from further testing and reduces laboratory animal use.

- Use of cell culture or molecular biology in preliminary studies of basic mechanisms of cardiovascular disease. An example is the use of an immortal cell line in molecular research on the effects of oxygen on the chemotactic response of macrophages to oxygen, reducing the need for whole animal studies.

- Development of fish (rainbow trout, zebra danjo fish & medaka) as predictive models for epigenetic carcinogens has reduced mammalian animal use in carcinogenesis studies.

- Development of an *in vitro* test for cytoadherence by malaria-infected erythrocytes to human melanoma cells, umbilical vein cells, and endothelial cells greatly reduces the need for nonhuman primates.

- Development of a SCID (severe combined immunodeficiency disease) mouse model where transplanted human liver tissue, a target for malarial sporozoite infection, can not be rejected, permits the evaluation of potential malarial vaccine candidates in a non-monkey model.

- Development of an *in vitro* drug screening system using infected human cells to replace the mouse malaria lethality model, eliminating the need for 4000 mice per year.

- *In vitro* drug screening, drug release kinetics, etc., result in reduction of drug candidates for numerous toxins reducing *in vivo* testing in rodent models up to 90% in some studies.

- Significant effort to develop DNA probes to detect *Rickettsia tsutsugamushi* in mammalian (including human) and chigger tissues should result in a 50% decrease in animal use for isolation and detection of this infectious agent.

- Development of an *in vitro* cultured human hepatoma cell line to assess radical and curative prophylactic activity of antimalarial drugs is in progress. This has the potential to reduce the number of monkeys needed for assessing antimalarial drugs and related compounds.

- *In vitro* techniques using human bone marrow cell culture to demonstrate propagation of Dengue viruses in these cells have reduced the number of monkeys needed for viral propagation by 25%.

- Development of a mosquito model using *in vitro* Dengue antigen detection techniques to pre-screen Dengue candidate vaccines should reduce the number of nonhuman primates needed for evaluation of vaccine candidates.

- Development of a reliable cell culture system for evaluating *Rickettsia tsutsugamushi* antibiotic resistance has reduced the need for animals for drug resistance studies by 50%.

- DNA probes have been developed to screen human *E. coli* isolates for pathogenicity. Only those positive to *in vitro* screening are tested in animals to confirm pathogenicity; this greatly decreases the numbers of animals used.

- Use of ELISA (enzyme linked immunosorbent assay) tests as a first screen in cellular mediator (interleukin 1) studies has reduced the number of mice previously required by 90%.

- The nervous systems of invertebrate sea slugs are used to study the effect of chemical and toxic agents on the electrical properties of nerve cells. This preliminary work reduces the number of vertebrates needed for subsequent study.

- Development and use of amphibian models (*Xenopus laevis* - frog) for assessing teratogenesis assays significantly reduce mammalian animal use.

#### **IV.2.2.B Reduction by substitution of *in vitro* or *ex vivo* methods**

- Synthetic *in vitro* or *ex vivo* systems like artificial bimembrane layers, cell or tissue culture systems, and isolated diaphragm muscle preparations replace or reduce the need for live, whole animal experiments in medical chemical defense research.

- Perfection of an *in vitro* method for growing *Plasmodium falciparum* (the most important human malaria that affects only man and certain monkey species) in human red blood cells has greatly reduced the number of nonhuman primates needed for this research.

- Development of specialized insect and vertebrate cell lines have reduced the need for intracerebral inoculation of suckling mice for the isolation of arboviruses.

- Use of transformed (immortal or self-propagating) cell cultures as an alternative to primary cell cultures that require frequent harvesting of tissues from animals.

- The use of monoclonal antibodies from hybridoma cells to replace animal-derived polyclonal antibody preparations greatly reduces animal requirements.

- *In vitro* techniques to orally infect mosquitoes with Dengue viruses have reduced the number of mice and monkeys needed for viral propagation by 25%.

- Training programs for urology residents utilizing lasers for bladder treatments are initially performed with pig bladders purchased from a processing plant. This reduces the number of animals used for surgical training.

***IV.2.2.C Reduction by substitution of another species of animal, or human volunteers as protocols progress into human trials***

- Studies have been performed to develop mouse and guinea pig models to replace the monkey as an aerosol model for botulism, staphylococcal enterotoxin B, and plague intoxication, which greatly reduces the number of monkeys needed for biological product toxicity and protective efficacy testing.

- Progression of a model of anti-malaria protective immunity into humans, where protective immunity is induced in human volunteers by injected irradiated malarial sporozoites, has reduced the need for animal use in malaria research.

- Although cynomolgus monkeys are the only known model for Hepatitis E infection, rats, lesser bandicoots (rat-like animal) and swine are being evaluated as alternate models to reduce the need for monkeys.

***IV.2.2.D Reduction by substitution of computer simulations or other technologies***

- Use of bioengineering tools to measure physiological parameters on human subjects in operational and experimental gravity (G) tolerance environments may result in a decrease in the number of animals currently used in G tolerance work.

- A research effort is aimed at developing physiological-based, computer models/algorithms to predict *in vivo* distribution, uptake, and elimination of toxic chemicals, thus reducing the need for animals.

- Development of a computer model simulating *in vivo* absorption, distribution, metabolism, and toxic effects of nerve agents and vesicants and validated against *in vivo* pharmacokinetics data in guinea pigs for the nerve-agent soman will significantly reduce the number of animals used in nerve-agent research.

- Training of professionals by interactive videos and innovative teaching techniques, e.g., laparoscopic instruments on sponges, reduces the use of animals.

- Integration of mathematical modeling and aeromedical cardiovascular nonhuman primate research should reduce animal use.

- A computer modeling program reduces the use of sheep in weapon blast overpressure research.

- A computer modeling program that identifies active sites on large molecular weight toxin molecules for intervention with therapeutic drugs is underway. This effort will substantially reduce the numbers of animals used in biotoxin studies.

### **IV.2.3 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.

#### ***IV.2.3.A Refinement to protocols that reduce pain***

- *Ex vivo* cardiovascular response studies (using tissues in isolated systems) of toxins, eliminate potential pain and distress for animals that would be used in whole animal systems.

- Refinement of methodologies associated with the feeding of arthropod vectors (chiggers) on rodents reduces discomfort to the animals. Use of an unobtrusive barrier system to prevent escape of the chiggers eliminates the need for the attachment of a cumbersome feeding capsule on the anesthetized animal.

- Studies performed to compare less reactogenic adjuvant regimens and alternative sites to foot pad injections in guinea pigs for evaluating hypersensitivity reactions (inflammation and swelling) from candidate Q Fever vaccines decrease potential discomfort associated with evaluation of vaccine candidates.

- Sophisticated technology such as Nuclear Magnetic Resonance Imaging is used to follow biochemical changes occurring over time in rats and other animals. This non-invasive procedure results in the use of far fewer animals and a more physiologically normal model.

- Development and evaluation of micro-encapsulated, time-released anesthetics and analgesics potentially beneficial to casualties on the battlefield have been performed. If perfected, these compounds will provide long-acting analgesia or anesthesia for animals on research projects where anesthesia or analgesia is not currently feasible.

- An evaluation of the feasibility and effectiveness of using topical analgesia (pain relief) on rabbits in Draize eye irritancy testing, and in systemic analgesia during Sereny' Testing (inflammation bioassay) on guinea pigs was performed. This provides the ability to perform a test while decreasing pain and distress without altering the outcome.

- A transdermal (applied to the skin) delivery system of analgesia to relieve pain in dogs was evaluated. Provides an extended analgesia or anesthesia for animals on

research projects, and will be of benefit in human and veterinary medicine for the relief of pain.

#### ***IV.2.3.B Refinement to protocols that reduce distress***

- Development of telemetric surgical procedures for implantation of sensors, allows non-stressful measurement of clinically relevant physiological parameters in non-clinical vaccine and drug efficacy studies. This not only decreases stress associated with manipulative measurements, but the radio-transmitted measurements vastly improve the quality and quantity of data available. Additionally, use of the telemetry allows physiological assessment for efficacy trials, makes intervention with analgesia more feasible, and significantly reduces the use of lethality as the primary endpoint.

- Video tapes are used for adjunct training of technicians and investigators for common animal use procedures, i.e., venipuncture, handling, restraint, etc.

- Novel antibody production and collection techniques in rabbits and goats with plasma collection chambers reduce potential distress associated with venipuncture procedures and reduce, and, in some cases, eliminate immunoadjuvant use.

- Use of slings for studies requiring restraint of pigs and extensive conditioning of the swine prior to initiation of the study result in a significant refinement by reducing potential distress.

- DoD facilities use social housing systems, e.g., multiple animal housing or gang caging, where feasible, which expand intraspecies interactions, and use environmental enrichment strategies that extend to many species that are not specifically mandated by animal welfare legislation. These housing strategies increase the quality of life for the animals.

- A flexible polyethylene mesh restraint device that is more comfortable and is well tolerated by rodents replaces the use of rigid restrainers previously used for maintenance of arthropod (mosquito) vectors.

- A project is underway that plays back natural nonhuman primate vocalizations and analyzes the effectiveness of this as an environmental enrichment strategy.

- Development of a hyphema (fluid in the anterior chamber) model in rabbits has been using a non-invasive laser beam to open intraocular vessels and to create the hyphema instead of the standard surgical procedure previously required. This procedure eliminates post-surgical distress.

- Study endpoints are adjusted to reduce the need to proceed to death as a defined protocol objective. An example is the evaluation of the neurotoxicity of

candidate therapeutic radioprotective compounds in mice using decrements or changes in motor behavior and coordination as a definitive endpoint rather than death.

- A non-lethal model of botulism that detects intoxication by sciatic nerve paralysis in mice is under development and will be a significant refinement to the current mouse bioassay.

#### ***IV.2.3.C Refinement in research models and animal alternatives***

- Professional biostatisticians are used by IACUCs to collaborate with scientists on experimental design and to review proposals in committee to ensure that only the minimal numbers of animals needed for statistical validity are approved for use.

- Extensive use of purpose-bred, e.g., nude mice, hairless guinea pigs, etc., microbiologically and genetically defined, research animals yields better animal models and more meaningful and relevant research results.

### **IV.3. 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. Animal use alternatives including refinement, reduction, and replacement constitute key initiatives in the biomedical research, testing, education, and training programs of the Department of Defense. The number of large animals used by the military departments over the past decade has been very significantly reduced and some large species are rarely used at all.

## SECTION V

# ANIMAL USE OVERSIGHT AND PROCEDURES TO AVOID UNINTENDED DUPLICATION OF RESEARCH AND UNNECESSARY RESEARCH

---

---

This section responds to the House Armed Services Committee's direction that the Secretary of Defense describe animal use oversight and procedures to avoid unintended duplication of research and unnecessary research. Accordingly, this section speaks to the Military Department's mechanisms and procedures for oversight, management and direction of research planning and the actual conduct of research requiring the use of animals as subjects. For the purposes of this report and consistent with the President's National Defense Budget Request, research is defined as those Congressionally authorized science and technology (S&T) base activities - *Title II, Research, Development, Test and Evaluation (RDT&E)* - of the Military Departments, and for which funds are appropriated, within program elements 6.1 (Basic Research), 6.2 (Exploratory Development) and 6.3 (Advanced Development).

### **V.1. DETERMINATION OF DEPARTMENT OF DEFENSE (DoD) NEEDS FOR ANIMAL RESEARCH**

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

Each Defense research laboratory tailors its organization, staffing, and related infrastructure within available resources to best meet its S&T mission and to support each Commander's accountability, responsibility and authority. Although the specific elements and processes of individual protocol review may differ, the general process is summarized as follows.

An investigator develops a research protocol in support of Departmental S&T guidance and other supplementing guidance 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 of the Defense Technical Information Center (DTIC) database. DTIC maintains a database of ongoing and completed research at the work unit level of detail. Prior to initiation of an in-house or extramural Defense research project, a DTIC database search must be completed to verify non-duplication of previous or on-going research. Review and certification that this requirement has been met are conducted differently by each Service, and are integral elements of the

review and approval process for initiating a research project. While work units must address the requirement for a DTIC search, protocols also routinely incorporate information from other automated and on-line databases (i.e., Medline, AGRICOLA, Toxline, etc) and the scientific literature and knowledge gained through participation in scientific meetings, symposia, and workshops of other on-going or completed research. For research requiring animals, the Institutional Animal Care and Use Committee (IACUC) requires two specific elements to be addressed. First, in accordance with the Animal Welfare Act, specific databases must be reviewed for alternatives to painful procedures. Additionally, protocols submitted to an IACUC must contain reviews of the current literature to document the necessity for use of animals in the protocol and to prevent duplication of research.

Since protocols require the utilization of Defense resources, individual protocols are routinely subjected to review for factors such as military relevancy, necessity, scientific merit, and relative research priority. Such reviews are normally conducted within the laboratory's command-and-control structure and are routinely characterized by the features of peer review systems.

The facility's IACUC functions to review all new research protocols involving the care and use of animals to ensure that: (a) it is based on sound scientific principles, (b) the number of animals used is the absolute minimum required to achieve the purpose, (c) the lowest species of animal is selected as the appropriate model, (d) there is appropriate use of analgesics and anesthetics, if required, and if not used, there is adequate justification, (e) the research is not duplicative, (f) the personnel conducting the research are qualified by training and experience to conduct the research, and (g) the scientific question to be answered is of sufficient importance to warrant the use of animals.

## **V.2. OVERSIGHT OF ANIMAL CARE AND USE FACILITIES**

There are three major oversight agencies for animal care and use programs at DoD research facilities: Military Inspection agencies, IACUC and the American Association for Accreditation of Laboratory Animal Care (AAALAC).

### **V.2.1 Military Departments Agencies**

Each Military Department has a component or components responsible for routine inspection of its research facilities. The inspections are conducted formally and reports are prepared.

The Army's ultimate oversight responsibility is divided between two major commands--the U.S. Army Medical Command (Provisional) and the U.S. Army Materiel Command. Subcommand staff actually perform the inspections. In the U.S. Army Medical Command (Provisional), inspections are accomplished by veterinarians in the U.S. Army Medical Research, Development, Acquisition, and Logistics Command (Provisional) (Animal Use Officer) and the U.S. Army Medical Department Center and School (Veterinary Programs Manager). In the U.S. Army Materiel

Command, inspections are accomplished by a veterinarian assigned to the U.S. Army Chemical and Biological Defense Command. Ultimate oversight responsibility in the Navy resides in the Office of the Surgeon General of the Navy. The oversight is accomplished through the Naval Medical Research and Development Command, the Health Services Education and Training Command (Clinical Investigations), and the Inspector General at the Naval Bureau of Medicine and Surgery. Air Force oversight is accomplished by the office of the Director of Medical Inspection, Air Force Inspection Agency.

### **V.2.2 IACUC**

A common research review element of all research laboratories in which animals are used as subjects of research is the IACUC's review of the research protocol. DoD Directive 3216.1 requires that all DoD facilities using animals in research comply with the Animal Welfare Act. The Animal Welfare Act requires the Chief Executive Officer to appoint an IACUC, qualified through the experience and expertise of its members, to assess the research facility's animal program, facilities, and procedures. Forty of 45 DoD operated animal use sites have established their own IACUC to review all proposed animal uses to ensure compliance with the Animal Welfare Act. Of the five sites without an IACUC, three sites have such low animal use that they submit their protocols to their parent organization for review; one site is collocated at Wright-Patterson Air Force Base and uses its IACUC; and one facility does not use live animals.

Each IACUC is chaired by a highly qualified individual. The backgrounds of the chairpersons of these IACUCs are identified in Appendix E. The Animal Welfare Act requires an IACUC have at a minimum three members. DoD IACUCs had an average of eight committee members each. In addition, each IACUC has at least one Doctor of Veterinary Medicine member with training or experience in laboratory animal science and medicine.

The Animal Welfare Act further requires that at least one member of the IACUC not be affiliated with the institution in any way other than as a member of the Committee. This individual cannot be a member of the immediate family of a person who is affiliated with the facility, and this individual is expected to provide representation for general community interests in the proper care and treatment of animals. This outside member can perform unannounced site visits and participates in all discussions and votes on all protocols. All 40 IACUCs had a community representative on their committee. All IACUCs reported that selection of this community representative was made to ensure that the individual represents the community interests.

The IACUC is responsible for assessing the research facility's animal care program, the research facilities, and the facility procedures. There are eight Federally-mandated IACUC functions. At least once every six months, it reviews the research facility for humane care and use of animals and inspects all the animal facilities, including animal study areas and satellite facilities. The IACUC must prepare written

reports of its evaluations and submit the reports to the Institutional Official (facility commander for DoD facilities) of the research facility. These reports need to specifically address compliance with the Animal Welfare Act, to identify any departures from the Act, and to include an explanation for this departure. The report must distinguish between significant and minor deficiencies. All DoD IACUCs document their meetings and activities, including the results of inspections, complaints, actions, and training. They review and investigate concerns involving the care and use of animals at the research facility resulting from complaints received from the public and from reports of noncompliance received from laboratory personnel. To facilitate the reporting of complaints or concerns, facilities commonly place signs in public areas and in animal study areas advising both the public and personnel who work with animals how to contact members of the IACUC and/or the Inspector General (IG) whenever an issue of humane treatment of animals arises. Facilities reported a wide variety of proactive efforts to both inform the public on how to contact responsible individuals as well as programs to ensure that those who work with animals are fully apprised of the requirement to provide humane and ethical care (Appendix F). Additionally, IACUCs are mandated to make recommendations to the Institutional Official regarding any aspect of the research facility's animal program, facility, or personnel training; review and approve, require modification to, or withhold approval of new research protocols involving the use of animals; review and approve, require modification to, or withhold approval of proposed significant changes regarding the care and use of animals in ongoing research protocols; and suspend an activity involving animals when they determine that the activity is not being conducted in accordance with the approved protocol.

In addition to the oversight functions of the IACUC, the DoD provides extensive veterinary and animal care services for DoD facilities. Veterinarians with specialization in laboratory animal medicine (LAM) direct the programs for animal care and use. These experts 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, current interpretations, and implementing regulations of the Animal Welfare Act. The DoD sponsors several programs for training veterinarians in LAM, including a nationally recognized four-year residency program and long-term civilian training in LAM culminating in either a masters or doctoral degree. Approximately 25% of the members of the American College of Laboratory Medicine participated in DoD sponsored training programs. In addition, the DoD also trains animal care specialists (Military Occupation Specialty 91T) that assist in the daily care and treatment of laboratory animals. Over the last 26 years, the DoD has trained over 3000 animal care specialists. The DoD research institutions also send laboratory staff members to workshops sponsored by the National Institutes of Health, other Federal agencies, and private institutions dedicated to the proper use of research animals.

The IACUCs actively provide informational material to all members including the non-affiliated member to ensure that each member is fully knowledgeable on the humane care and treatment of animals. All sites reported providing introductory and

continuous training to members including the community representative. The type of training provided to IACUC members is detailed in Appendix G.

The community representative, as well as other members of the IACUC, is encouraged to make *No Notice* visits to the research facility to evaluate the care provided to animals. All sites engaged in live animal research allow and encourage the members of the IACUC to make unannounced visits. Twenty-four unannounced visits were made by non-affiliated members during fiscal year (FY) 1993.

### **V.2.3 AAALAC**

This is a nonprofit organization to promote high quality standards of animal care, use and welfare through the accreditation process. Participation in the accreditation process is voluntary. The AAALAC accreditation process provides scientists and administrators with an independent, rigorous assessment of the organization's animal care and use program. Sixty percent of the animal care programs at the 45 DoD research, education, training, and testing facilities using animals are accredited. The AAALAC accreditation process is discussed in Section II.

### **V.2.4 Community Visits**

All facilities have a public affairs office, either at the facility or on the base, which can and does facilitate visits to the facility by the public and the press. During FY93 there were 28 such visits to DoD animal use facilities.

### **V.2.5 Additional Oversight**

Within the DoD, individuals may raise animal welfare concerns about the necessity of animal research with the IACUC, facility commanders, and the IG as well as with others, both within and outside (e.g., Waste, Fraud and Abuse Hotline) of the formal chain of command.

The purpose of the non-affiliated member and ombudsman is augmented by the Department's IG. An ombudsman is defined by 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 Committee on Armed Services, 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 all complaints regardless of their nature. These include but are not limited to personnel complaints, sexual harassment, animal welfare, etc. The DoD assigns this responsibility to its IG and respective Inspectors General of the Military Departments. In addition, military bases and large organizations on military bases have their own Inspectors General who fulfill this function.

As directed by DoD Directive 3216.1, all use of non-human primates requires an additional centralized review by a committee external to the research facility.

### **V.3. CHAIN OF COMMAND OVER ANIMAL CARE AND USE FACILITIES**

The chain of command is a system designed to resolve problems at the lowest possible level. It provides the control and communication between 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 each 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. Everyone in the military is a part of the chain of command. This report documents the various chains of command for each facility that uses animals in research. The chain of command for each facility using animals for research, education, testing and training is provided in Appendix H.

### **V.4. AVOIDANCE OF UNINTENDED DUPLICATION OF RESEARCH**

Both the DoD and the 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, joint planning and review of its research programs.

Congress, in 1981, 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 as 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 (JTTCGs), 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.

The ASBREM Committee process became the model for joint DoD coordination initiatives. Responsibility for joint coordination, planning, execution and review of the Departments' 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 V-1. Joint S&T 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 Committee is supported by the JTCGs (figure V-2) and the JDL is supported by separate technology panels.

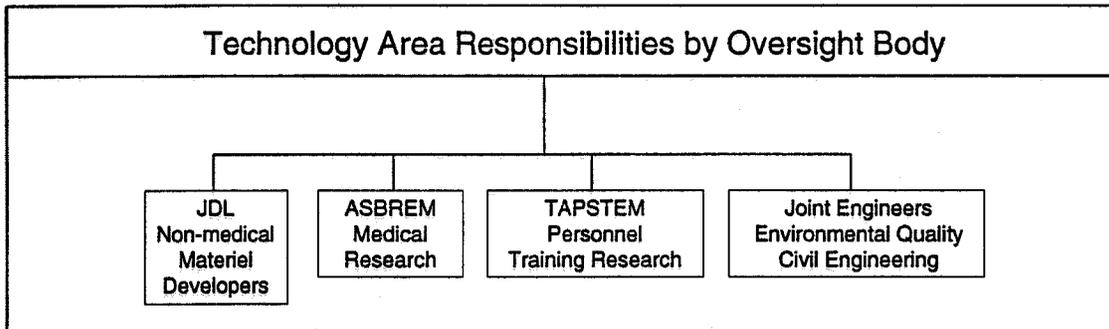


Figure V-1 DoD Technology Area Responsibilities

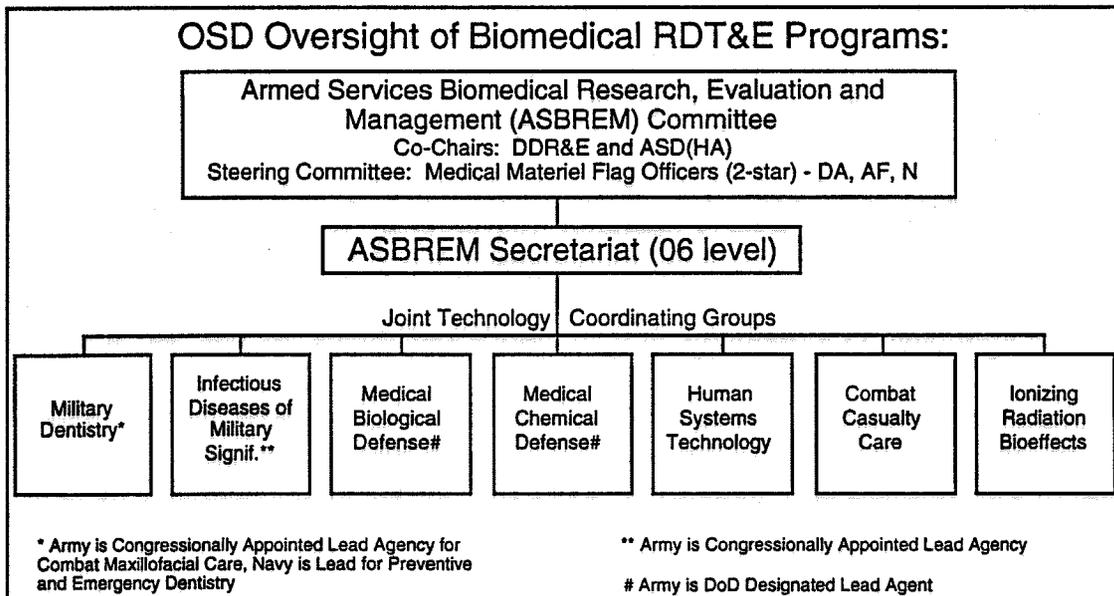


Figure V-2 Structure of Armed Services Biomedical Research, Evaluation, and Management Committee

#### V.4.1 Less Formal Disincentives for Unintended Duplication of Research

In addition to these more formal coordination and review processes to eliminate unintended duplication of research, 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 because of funding shortages. Professional stature of individual scientists or engineers among their peers is accrued in proportion to their individual and original contributions to the scientific literature. There is little if any reward for duplicating the work of others; such actions often have significant negative impacts 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 their individual scientific and technological contributions. This peer review system provides career and financial incentives to original contribution since it rewards the relative magnitude of the contributions and scientific impacts with eligibility for higher pay grades. One outcome of research is publication of a manuscript in a professional journal or presentation to a professional meeting. These peer-reviewed journals critique the research during the review process leading to an overall enhancement of the research process as well as validating the scientific merit and necessity of the research. During FY93 there were more than 1400 animal-based research publications and presentations accepted by non-DoD professional peer groups and over 120 publications and presentations made to DoD groups alone. Appendix I lists representative journals in which the DoD published articles that resulted from animal 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. These are but a few of the many less formal considerations that provide substantial individual and institutional barriers against unwarranted duplication of research.

## **V.5. AVOIDANCE OF UNNECESSARY RESEARCH**

The same factors that effectively prevent unwarranted duplication of research are also applied to prevent unnecessary research. Additionally, through Cooperative Research and Development Agreement mechanisms, the Department has increased its emphasis on leveraging and exploiting for Defense needs, the S&T investments by other Federal agencies, U.S. industry, and academic institutions, as well as by 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 the Defense S&T strategy is application of S&T accomplishments to sustain Defense technological superiority through efficient and responsive modernization of our warfighting capabilities.

## **V.6. SUMMARY**

Research performed by the DoD is reviewed, both formally and informally, by various offices and committees before it is funded or implemented. These reviews serve to determine the necessity to the mission, oversight of animal use and avoidance of unintended duplication of research. Over the past decade the DoD, with the Congress, has streamlined and greatly improved coordination of its S&T activities so as to avoid unnecessary duplication and to provide a focused program of research responsive to the DoD's needs. The IACUC is responsible for the oversight of animal care and use and also prevents unwarranted duplication of research involving animals. Each DoD facility's IG is an effective means of investigation for concerns about the necessity of animal use, as well as the ethical treatment and humane care of animals used in DoD research. Additionally, the IACUC provides training and

information about animal care and use, and assures the humane use of animals in research.

## 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.

**American Association for Accreditation of Laboratory Animal Care (AAALAC):** A voluntary private organization that, by April 1985, provided accreditation for 483 institutions. AAALAC accreditation is based on the provisions of the NIH *Guide for the Care and Use of Laboratory Animals*, and is recognized by the Public Health Service.

**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, 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 Care and Use Committee (ACUC):** See Institutional Animal Care and Use Committee (IACUC).

**Animal Use:** The use of animals for research purposes. Three aspects of animal use are dealt with in this assessment: in behavioral and biomedical research; in testing products for toxicity; and in the education of students at all levels. This assessment does not cover animal use for food and fiber; animal use to obtain biological products; or animal use for sport, entertainment, or companionship.

**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 USDA. Animals covered by the act, as currently enforced, are dogs, cats, hamsters, rabbits, guinea pigs, nonhuman primates, and marine mammals.

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

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

**Biological Testing:** The repetitive use of a standard biological test situation or protocol employing different chemicals or different test parameters. Such test protocols are more stereotyped than those used in research, and may be more amenable to the institution of a computerized data retrieval system.

**Biomedical Research:** A branch of research devoted to the understanding of life processes and the application of this knowledge to serve humans. 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.

**Blast Overpressure:** The concussion that results when weapons such as artillery pieces are fired. Soldiers firing these weapons can be severely injured by the local pressure effects resulting from weapon use.

**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.

**Carcinogenesis:** The process by which a change to a cell occurs that leads to cancer.

**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.

**Chemotactic:** To attract by release of a chemical. For example, cells are attracted to a site of tissue damage by the release of chemicals by the injured cells.

**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 product 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.

**Draize Eye Irritancy Test:** A test that involves placing a single dose of a test substance into one eye of four to six rabbits (the other eye remains untreated) and observing its irritating effects. A promising alternative to this test is the chick embryo chorioallantoic membrane assay.

**Education:** The aspect of education dealt with in this assessment is the use of animals and alternatives in the teaching of life sciences to health professionals and preprofessionals, and research scientists.

**ELISA (Enzyme Linked Immunosorbent Assay):** An assay system that uses antibodies conjugated to enzymes. The amount of antibody attached to the molecule being analyzed can be detected by adding compounds that are cut by the enzyme releasing a colored product which can be quantified.

**Ex Vivo:** Outside the living body: denoting removal of an organ, tissue or cells.

**Guidelines for Animal Care and Use:** Various organizations outside the Federal Government have adopted their own guidelines -- e.g., the APA's *Guidelines for Ethical Conduct in the Care and Use of Animals*, which is the most comprehensive and has been endorsed by FASEB; the APS's *Guiding Principles in the Care and Use of Animals*; and the AVMA's *Animal Welfare Guiding Principles*. For Federal guidelines, see Interagency Research Animal Committee, NIH *Guide for the Care and Use of Laboratory Animals*, and PHS *Policy*.

**Institute for Laboratory Animal Resources (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 percent of the Earth's nonplant species. For the purposes of this assessment, invertebrates are not considered to be animals.

**In Situ:** In position.

**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.

**Macrophage:** A white blood cell that is very active in inflammatory responses and in engulfing foreign objects such as bacteria.

**Microorganism:** A minute microscopic or submicroscopic living organism, such as bacteria, viruses, and protozoa.

**Mutagen:** An agent that induces chemical changes in genetic material. Chemicals, viruses, and ionizing radiation can be mutagenic. Most carcinogens are mutagens, therefore many screening tests to detect carcinogens are designed to detect the mutagenic potential of the compound. Some mutagens are not direct-acting, requiring metabolic activation in the body before they exert their mutagenic potential.

**NIH Guide for the Care and Use of Laboratory Animals:** Revised in 1985, the *Guide* lays out detailed standards for animal care, maintenance, and housing. Its provisions apply to all research supported by NIH, and it is used by most animal research facilities, both within and outside the Federal Government. AAALAC and PHS also use it when assessing research facilities for accreditation.

**Nonliving Systems:** Inanimate chemical or physical systems used in testing.

**Oncology:** The study of tumors.

**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.

**PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions:** Revised in 1985, the *Policy* applies to PHS-supported activities involving animals (including those of NIH). It relies on the *NIH Guide for the Care and Use of Laboratory Animals*, and uses institutional committees for the assessment of programs and maintenance of records.

**Polymerase Chain Reaction:** A molecular biological system in which pieces of genetic material can be synthesized in large amounts *in vitro*. This material can be

used in diagnostic testing, genetic studies, or for a large number of molecular biological purposes.

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

**Reduction:** Considered an alternative to animals 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 subject 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, however.

**Sporozoite:** The infectious stage of the malarial parasite that is transmitted by mosquitoes.

**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.

**Toxicity Testing:** The testing of substances for toxicity in order to establish conditions for their safe use. There are now more than 50,000 chemicals on the market and 500 to 1,000 new ones are introduced each year.

**Vesicant:** A chemical agent that causes burns and tissue destruction both internally and externally.

**Veterinary Medicine:** The maintenance and improvement of the health and well-being of animals, particularly the 30 to 40 different species of animals of economic, ecological, and environmental importance. Veterinary medicine is closely allied with veterinary research.

SECTION VII  
REFERENCES  
(IN ORDER OF CITATION)

---

---

National Defense Authorization Act for Fiscal Year 1993, Report of the House Armed Services Committee, H.R. 5006, May 19, 1992

Department of Defense Directive 3216.1, "The Use of Animals in DoD Programs," February 1, 1982

Title 7, United States Code, Sections 2131-2156, The Laboratory Animal Welfare Act of 1966, PL 89-544, as amended PL 94-279, 1976, and PL 99-198, 1985

U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication No. 86-23, Guide for the Care and Use of Laboratory Animals, Revised 1985

Weichbrod, Robert H. (1993) Animal use in the Department of Defense research facilities: An analysis of "Annual Reports of Research Facilities" filed with the U.S. Department of Agriculture, 1986-1991. University Microfilms Inc., Walden University Institute for Advanced Studies

Joint Regulation (Army Regulation 70-18; Secretary of the Navy Instruction 3900.38B; Air Force Regulation 169-2; Defense Advanced Research Projects Agency Instruction 18; Defense Nuclear Agency Instruction 3216.1B; Uniformed Services University of the Health Sciences Instruction 3203), "The Use of Animals in DoD Programs," June 1, 1984

Review of Animals in the Department of Defense Medical Research Facilities, Inspector General Department of Defense, (1994)

Medical Science and Technology Master Plan, U.S. Army Medical Research and Development Command, 1994

Russell, W.M.S. and Burch, R.L., "The Principles of Humane Experimental Technique," Charles C. Thomas Publishers, Springfield, IL, 1959

Army Science and Technology Master Plan, Fiscal Year 1994. Department of Army, November 1993

Title 9, Code of Federal Regulations, Animals and Animal Products, Chapter 1, Animal and Plant Health Inspection Service, Subchapter A - Animal Welfare; Source: 54 FR 36147, August 31, 1989

*References*

---

H.R. 96-1317, Department of Defense Appropriation Bill, 1981; Representative Addabbo, House Committee on Appropriations; 96th Congress, 2nd Session September 11, 1980

H.R. 97-332, Department of Defense Appropriation Bill, 1985; House Committee on Appropriation; 99th Congress, 1st Session October 24, 1985