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A REVIEW OF THE TOXICOLOGY RESEARCH
PROGRAM OF THE 6570TH AEROSPACE
MEDICAL RESEARCH LABORATORY,
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

National Research Council

Prepared for:

Office of Naval Research

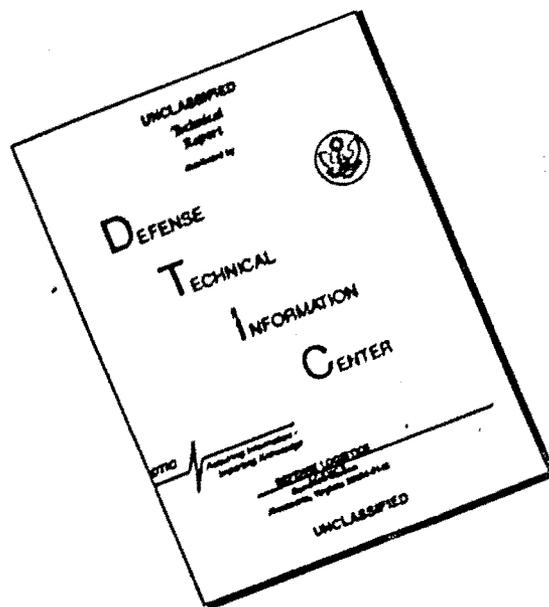
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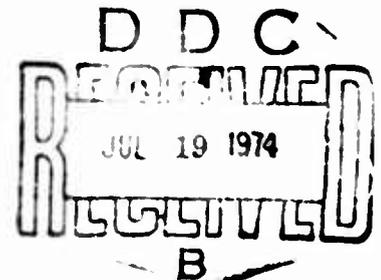
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A Review of the Toxicology Research Program

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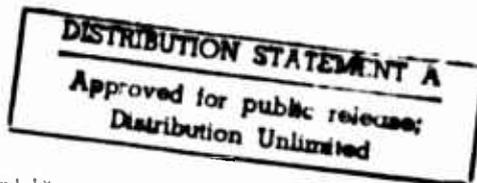
**6570th Aerospace Medical Research Laboratory
Wright-Patterson Air Force Base
Ohio**

June 1974



National Academy of Sciences-National Research Council

A report of the Committee on Toxicology, Bertram D. Dirman, Chairman, under Contract No. N00014-67-A-0244-0015 with the assistance of an ad hoc Sub-committee chaired by Frank G. Standaert.



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16. Abstracts

In response to a request from the Air Force, the Committee on Toxicology of the National Academy of Sciences-National Research Council, with the assistance of a specially appointed ad hoc Sub-committee, reviewed the toxicology program at Wright-Patterson Air Force Base. It concluded that there is good reason for the Air Force to maintain an independent laboratory for toxicology research. It found that toxicology evaluation program to be functioning well and providing information and services adequate for Air Force needs. It reported that the methods are appropriate, the research is productive, and the program is relevant to the Air Force needs.

The Sub-committee believes that the use of animals, including dogs, is necessary for the development of scientific information to protect military and civilian personnel and the general public because there are, as yet, no adequate alternatives to the use of animals for toxicologic research. It found the practices and procedures for the use of animals by the 6570th Aerospace Medical Research Laboratory (AMRL) to meet or exceed all standards for proper and humane care.

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Preface

The following report of a review of the toxicology research program at the U.S. Air Force 6570th Aerospace Medical Research Laboratories is presented by the Committee on Toxicology of the National Academy of Sciences-National Research Council; it was prepared with the assistance of an ad hoc Sub-committee.

The Committee and its Sub-committee are pleased to acknowledge the financial support, provided under contract N00014-67-A-0244-0015, which made this study possible. They extend their thanks for assistance and cooperation from the staffs of the Secretary of the Air Force, the Surgeon General, the Aerospace Medical Division, and the 6570th Aerospace Medical Research Laboratories.

The Committee on Toxicology of the National Research Council expresses its sincere appreciation to Dr. Standaert and to the other members of the Sub-committee for their willing assistance in the preparation of the report.

Special thanks are due to the Society of Toxicology for the independent review of this report by Messrs. Borzelleca, McCollister and Weil.

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Summary

A. General Statement

In response to a request from the Air Force, the Committee on Toxicology of the National Academy of Sciences-National Research Council, with the assistance of a specially appointed ad hoc Sub-committee, reviewed the toxicology research program at Wright-Patterson Air Force Base. It concluded that there is good reason for the Air Force to maintain an independent laboratory for toxicology research. It found that toxicology evaluation program to be functioning well and providing information and services adequate for Air Force needs. It reported that the methods are appropriate, the research is productive, and the program is relevant to the Air Force needs. It noted that the Air Force has established cooperative programs with other federal and civilian agencies to avoid duplication of effort on common problems. It suggested that some auxiliary functions, e.g., the advisory function and fundamental research, could be strengthened.

The Sub-committee believes that the use of animals, including dogs, is necessary for the development of scientific information to protect military and civilian personnel and the general public because there are, as yet, no adequate alternatives to the use of animals for toxicologic research. It found the practices and procedures for the use of animals by the 6570th Aerospace Medical Research Laboratory (AMRL) to meet or exceed all standards for proper and humane care. It concluded that the species are selected on the basis of sound scientific and economic reasons, and the experiments provide data that are unavailable elsewhere.

In pragmatic terms the Sub-committee noted that the laboratory at Wright-Patterson Air Force Base is one of the major toxicology research units in the United States. The demands of past projects have brought experienced and capable scientists to this unit. These tasks also caused the creation of the "Thomas Domes," which are large exposure chambers equipped with sophisticated means for controlling the environment and regulating the material to which the animals are exposed while observing and recording their responses to exposure. These facilities are equal to any in the world. The Sub-committee suggested the Air Force determine whether the facilities are being used to their full potential.

An analysis of the findings of the Committee and its Sub-committee follows:

B. Strengths

1. The great strength of this facility is the equipment for conducting inhalation toxicity studies with rigorous control of the atmosphere and full monitoring of subjects. Research installations of this type are few in number, and extremely difficult and expensive to create.

2. The animal quarters and the facilities for quarantining and processing animals are excellent. They are staffed by personnel who are well trained and highly motivated.

3. The procedures for animal procurement, quality control, care, and use match or exceed those of most biomedical research facilities in this country.
4. The staff of the Laboratory is experienced and capable.
5. The organizational framework and administrative support are well defined and managed.
6. Cooperation between the Air Force, other governmental agencies, and the contractor responsible for the operation of the facilities has been developed in a manner that provides flexibility and minimizes duplication of effort.
7. The Laboratory is well run and has been productive.
8. The advisory function for occupational safety and health of Air Force personnel is being carried out adequately, but could benefit from more formal procedures.

C. Areas in Need of Strengthening

1. An effort should be made to publish more in refereed journals, both to ensure quality of research and to make readily available the results of that research.
2. Wherever feasible, morphologic studies should be supplemented by analysis of other functions, including behavior, physiology, and reproduction.
3. Library and other technical information sources at AMRL are almost nonexistent.
4. Research outside of basic descriptive toxicology seems diffuse. It should be evaluated and strengthened, cut back or focused.
5. The present system of program review is subject to the criticism that it comes from the Air Force or the contractor. It would be highly desirable to develop a system of periodic review by outside experts.
6. Procurement of animals should be through long-term contracts rather than by annual open-bid procedures. "Debarking" should not be an automatic specification.
7. Rapid turnover of military scientific personnel creates problems in continuity. It is also wasteful because it takes several years to develop a new program and the serviceman may leave before the new program becomes fully productive.
8. Methods should be found to encourage the scientific personnel to broaden their professional horizons and to prevent intellectual isolation and stagnation. The recent association with the University of California may provide a vehicle for this.
9. The present contract for histopathology is relatively small and seems capable only of providing routine slide work. Consideration should be given to either developing total in-house capability for histopathology or enlarging the contract to provide for on-site involvement.

D. Unknowns

1. University of California. The effectiveness of the interaction between AMRL and the University of California cannot be assessed at this time because the experience is too limited. It should provide the means by which the resources of the university can be drawn upon to answer specific questions of concern to AMRL. Furthermore, interaction between the University and AMRL should provide unique training in this specialized field for scientists on both sides. On the other hand, the University of California and its staff are so far away that there undoubtedly will be a problem of communication and one wonders how much the University faculty will interact with the ongoing work at AMRL.

2. Service to Other Agencies. AMRL seems to be inclined toward doing contract work for other agencies. In the Sub-committee's opinion the primary direction of the program should remain with the Air Force and its requirements should have first priority on the facilities. It is healthy to cooperate with other agencies, and to exchange information, providing that an upper limit is maintained. It would be a mistake to permit the amount of service to other agencies to grow to an extent that service to the Air Force would be hampered.

3. Intentions of the Air Force. There are many signs that a superb facility is being under-used. Although designed to deal with toxicological problems in space vehicles, the laboratory is eminently suitable for the environmental-impact and basic-research problems that are more pressing today. The Air Force should analyze its current and future needs for toxicology research and develop AMRL accordingly.

* * * * *

I. Background

A. Proximal Reasons for Review

During June 1973, the Air Force issued a procurement notice (Appendix 2) for the purchase of 200 Beagle dogs to be used in the toxicology research program at Wright-Patterson Air Force Base. The specifications required that the dogs be more than six months old, i.e., mature, and that they be "debarked," the latter being a jargon term for a minor surgical procedure performed under light anesthesia that temporarily reduces the loudness of a dog's bark. The contract was awarded in August.

This solicitation came to the attention of Congressman Les Aspin who requested information on the proposed use of the dogs and on other Air Force programs using animals (Appendix 3). The National Anti-Vivisectionist Society filed a lawsuit in U.S. District Court seeking to enjoin the Secretary of Defense and his subordinates from purchasing Beagles, or any substitute animal, for the purposes intended and from conducting environmental-pollution studies upon Beagles, or any substitute laboratory animal, or upon any human person without that person's freely given and knowing consent (Appendix 4).*

* U.S. District Court Judge Philip Tome dismissed the case on January 11, 1974 on the grounds that his court lacked jurisdiction.

B. Charge to Committee on Toxicology

The Deputy Surgeon General of the Air Force requested the assistance of the Committee on Toxicology in accordance with an inter-agency contract with the National Academy of Sciences (N00014-67-A-0244-0015) and the associated memorandum of agreement dated 26 June 1956 (Appendix 5). The Committee was asked to review the Air Force program for its adequacy, experimental methodology, and relevance to Air Force needs. The review was to determine if use of these animals would be consistent with animal-care practices and if the research program was necessary. The specific charge to the Committee was as follows:

1. Purpose: Review Air Force program for adequacy, experimental methodology, and relevance to Air Force needs.

2. Background: Concern has been expressed over the specific use of "debarked" Beagle dogs in the Air Force Toxicology Program. In order to determine that the use of these animals is not only consistent with animal-care practices but also necessary for research, a review of both practices and programs is needed.

3. Tasks:

a. Evaluate Relevance of Program:

- i. How does program fulfill Air Force needs?
- ii. What is the relationship of Air Force needs to national needs: i.e., what degree of duplication exists? How much should exist?
- iii. Are there alternate experimental approaches to provide Air Force required data?

b. Assess Experimental Methodology:

- i. Rationale for use of various species of experimental animals.
- ii. Experimental methods for use/treatment of animals.
- iii. Data acquisition; i.e., do the experiments provide required information?

c. Prepare written report on above.

The Committee and Panel accepted the charge with the understanding that it was not limiting and that they would be free to investigate and report on all aspects of the problem as they deemed appropriate.

II. Chronology of Review and Participants

The chairman of the Committee on Toxicology, Bertram D. Dinman, nominated an ad hoc Sub-committee to conduct the review and to prepare a report for consideration by the Committee on Toxicology and submission to the Air Force. The nominees were approved by the President of the Academy, Philip Handler. Their names and those of the Committee are given in the Preface.

A preliminary briefing on the Air Force programs was given to Dr. Frank G. Standaert, chairman of the ad hoc Sub-committee, and Mr. Ralph C. Wands, Director of the Advisory Center on Toxicology, on September 24. This was arranged by Major Dominic Maio, USAF, BSC, who was responsible for all contacts between the Sub-committee and the Air Force. The briefing was held in the office of Dr. Billy Welch (SAFILE) and was attended by representatives of the Office of the Surgeon General, USAF, and of the Aerospace Medical Division.

At the end of the meeting, Dr. Standaert asked that a summary of the material presented at the briefing be prepared for other members of the Sub-committee. He also asked for written information on the scientific and managerial staff of AMRL, the work the Laboratory had done in the past, bibliographies of articles published in recent years, technical summaries of work in progress and projected for the coming year, procedures for animal procurement and use, and other material relevant to the task of the Sub-committee. These were prepared by the Air Force and distributed to the Sub-committee during its inspection visit to Wright-Patterson Air Force Base. Additional documents were provided by the Advisory Center on Toxicology. Copies of all written materials will be sent to the Air Force as an addendum to this report. A list of these is appended (Appendix 6).

The Sub-committee made an inspection visit to AMRL on 3, 4, and 5 October, 1973. The formal agenda is given in Apperdix 7. Dr. Melby arrived in Cincinnati before the other members and spent the afternoon of 3 October inspecting the vivarium and familiarizing himself with the procedures for procurement, care, and use of animals. The members of the Sub-committee met in executive session on the evening of 3 October to discuss material in hand and to plan for interviews and inspections. During the next two days, the Sub-committee visited and inspected the facilities. Briefings were presented by command staff and technical descriptions were given by AMRL scientists. The Sub-committee questioned each speaker carefully and conducted interviews with other staff members during visits to the laboratories. Several laboratories were visited more than once.

After the interviews and inspections the Sub-committee met in executive session to discuss observations and to outline the report. Members were assigned specific sections to draft. These were collated by chairman Standaert, reviewed, and revised by the Sub-committee and submitted to the Committee on Toxicology.

An independent review of the Sub-committee's activities and its report was conducted at Dr. Dinman's invitation by an ad hoc Committee of the Society of Toxicology. Joseph F. Borzelleca, President of the Society, was the Chairman. The other members of this ad hoc group were Carrol Weil and Donald McCollister. Dr. Borzelleca accompanied the Sub-committee during its site visit to ensure that no pertinent information was overlooked in the final report.

III. Purpose of Air Force Toxicology Facilities

The Air Force has immediate, short-range, and long-range programs of weapons systems research, development, and deployment. Associated with each of these is a responsibility for protecting the health and safety of Air Force and civilian personnel. There is a similar responsibility to the public health and to the environment; Presidential directives require that Air Force policies and practices be consistent with such federal laws and regulations as the Occupational Safety and Health Act of 1970 and the various acts administered by the Environmental Protection Agency.

A. Roles

The Air Force has therefore two stated roles for a toxicology research program: (1) generating appropriate data through research and (2) providing expert advice on Air Force problems in toxicology.

Research: The mission of the Air Force calls for its personnel to use materials or to work in environments that are unknown in the civilian sector: thus, there are circumstances in which the Air Force cannot draw upon the pool of information on toxic hazards that has been accumulated for civilian products. In order to protect its personnel, it must acquire the needed information. Sometimes it may be advantageous to contract the needed research to an academic institution or to a commercial laboratory but there are circumstances in which it may not be desirable to do so. For example, the data may be needed urgently or the performance of the work may require special facilities that are not available to contractors. There are also occasions when the project is too small to warrant outside contracting or where the nature of the problem cannot be defined adequately in advance of pilot research. Finally, the nation's toxicology research system is not large enough to meet the demands that are being placed upon it and in the absence of its own capability there would be no assurance that the Air Force could get its work done. Therefore, the Air Force relies on its toxicology research effort to provide information and to maintain a sound base of scientific and technical knowledge.

In practice Air Force needs and programs are identified by headquarters. These are then examined by the Surgeon General and the Aerospace Medical Division, and priorities for research programs are established on the basis of the needs and of the knowledge already available. The studies by AMRL are carried out pursuant to these directives. They are intended to determine the potential adverse effects of Air Force materials and to study the mechanism of such toxicity as might occur. The results of such tests are used to protect people against over-exposure to the chemical and to establish appropriate therapeutic procedures if overexposure occurs.

Advisory: All who work with potentially hazardous materials need a source of reliable information on toxicity and the means of controlling it. The Air Force is no exception. Furthermore, there is a need for a central source to accumulate the toxicologic experience of the Air Force and to mesh it with the information of other military and civilian agencies, industrial, and private research groups. To meet these needs, the Air Force has designated AMRL as its center for toxicologic information. Directives and memoranda of agreement call for the coordination of its toxicology efforts with those of other military services and federal agencies having similar needs and interests.

B. Comment

The Sub-committee found no reason to challenge the need for in-house capability to study and advise on the possible toxicity of the ever-increasing number of chemicals used by the Air Force. Although some of the substances are also widely used by industry and other agencies, there are many that are unique to the Air Force.

While it might be suggested that civilian contractors could do the work more efficiently than an in-house laboratory, there is no reason to believe that this is always the case, and there is ample reason to believe that certain Air Force projects could not be done by any civilian organization unless that organization were to make a huge capital expenditure for the special equipment needed. The Sub-committee also agreed that the Air Force should have experts who are capable of translating laboratory data into practical guidelines for field personnel and that these individuals should be engaged in toxicologic research. Practical experience is a distinct advantage in understanding the conditions under which the data were obtained, judging its reliability, and making recommendations for its application to field conditions. The availability of laboratories also gives these advisers the capability of undertaking research to clarify ambiguities or to extend work so that it more nearly suits the needs of the Air Force program.

Thus the Sub-committee endorses the philosophy that led to the establishment of the unit at Wright-Patterson Air Force Base and assigned to it the joint tasks of conducting research and providing advice on toxicologic matters.

IV. Assessment of Program of Toxic Hazards Branch of AMRL

A. Administration and Personnel

1. Description

The Aerospace Medical Research Laboratory reports through the Aerospace Medical Division to the Surgeon General of the Air Force and the Secretary of the Air Force. Administrative control over its programs and budgets rests with the Aerospace Medical Division, which is headquartered at Brooks Air Force Base. The Commander of the AMRL, currently Colonel Doppelt, has immediate responsibility for all operations of the Laboratory (Figure 1) including those of the Toxic Hazards Division and the Veterinary Medicine Division, the subjects of this report.

Overall direction for the Toxic Hazards Division comes from a civilian employee, Dr. A. A. Thomas, who oversees a budget (FY 1974) of about \$1,800,000, exclusive of military salaries. Most of this, \$1,200,000, pays for a contract to operate the Toxic Hazards Research Unit (THRU) which conducts all inhalation toxicology work as well as the associated support, supply, and maintenance services. Dr. Kenneth Back is the resident contract officer. The contractor provides a scientific director and program manager at the Laboratory to supervise its staff and work. This position is occupied by Dr. J. D. MacEwen.

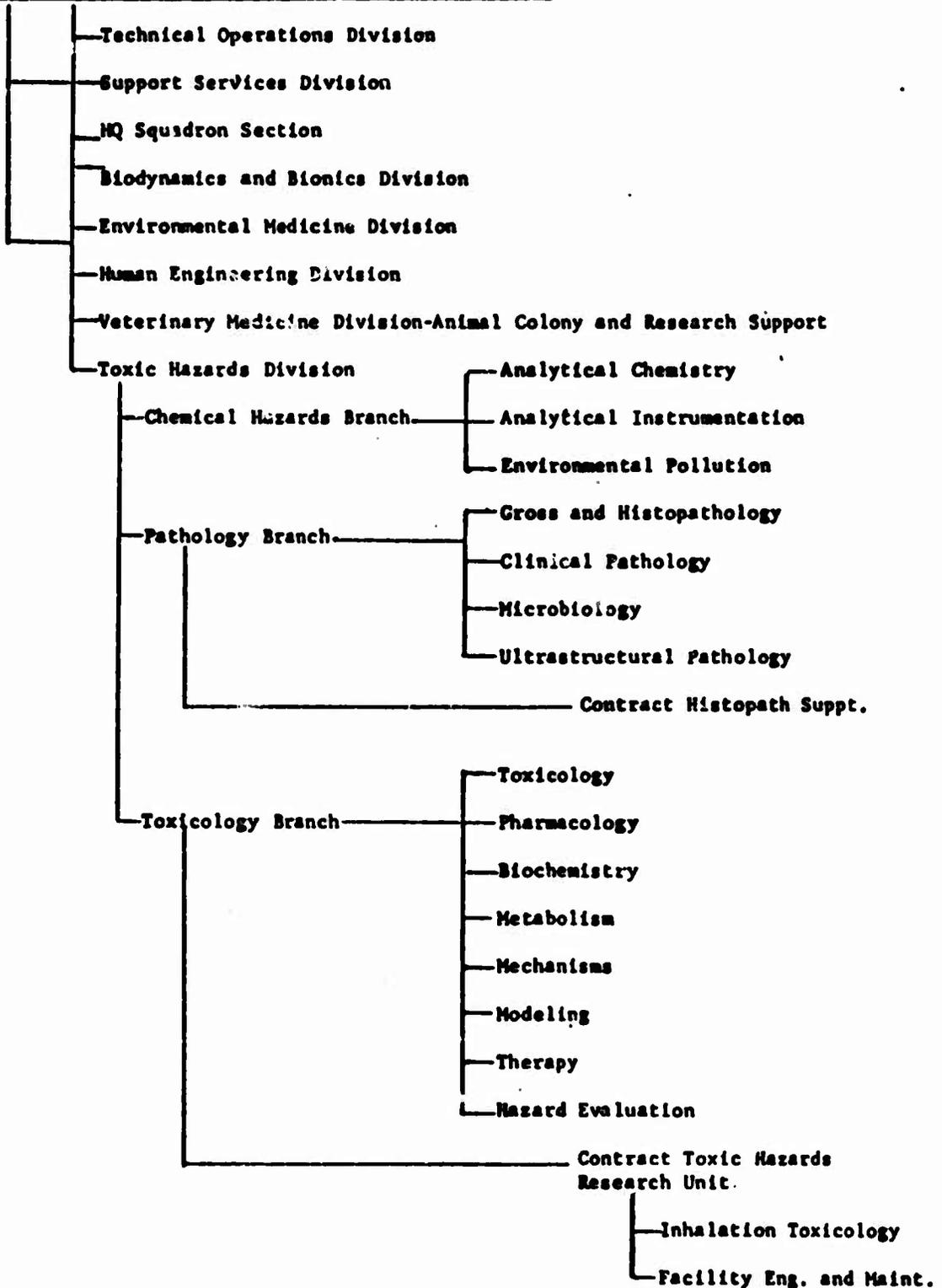
The laboratories have been operated under contract since their founding about ten years ago. The University of California (Irvine) was successful in the most recent bidding and was awarded a contract that runs from December 1972 to September 1976. The change of contractor will have little immediate effect on the operation of the laboratory since the contract, for which all bidders competed, required continuation of the key scientific personnel and projects of the laboratory. In addition to performing work at AMRL, the contractor is permitted to use up to ten percent of the contracted amount for related projects in his own facilities and he is permitted to send his students to work and study in the Air Force

AEROSPACE MEDICAL RESEARCH LABORATORIES

Organization and Functions

Aerospace Medical Division Commander

Aerospace Medical Research Laboratories Commander



Laboratory. The University is required to provide a scientific management team from among its own personnel for consultation and advice on research done under the contract. This group is charged with periodic program review and coordinating the activities at AMRL with those of supporting laboratories in California. It will meet about four times a year alternately at Irvine and Wright-Patterson.

2. Comment

The staffing of the Toxic Hazards Branch includes some arrangements that were considered excellent but others that seemed not to afford an optimal base upon which to support a research endeavor. Resumes of the staffs of the Toxic Hazards and Veterinary Medicine Divisions were made available to the Sub-committee (Appendix 6). Relatively brief personal contacts during the inspection visit confirmed the competence evidenced in these. The mixing of military and civilian personnel has been a successful arrangement over the years and there is ample evidence of close working relationships between the two groups. The senior scientists have long tenure and provide desirable continuity of programs and quality of performance as well as familiarity with the entire system. The administrative officers seem able and responsive.

On the other hand, flexibility of programs and new approaches to problems requires periodic infusion of new staff. Dependence on young medical officers who are putting in their two-year military service requirement time for significant portions of the programs may not optimally provide this; often they lack sufficient experience and continuity in the research projects in which they engage. At the time of the visit some of the areas were inadequately staffed and this seems to be a continuing problem. For example, the Sub-committee saw expensive facilities for neurophysiologic research but no investigator in that discipline. It also saw a recently acquired and expensive electron microscope and freeze cleave apparatus being used by an investigator whose two-year tour of duty ends in less than a year.

The role of the University of California deserves special discussion. Current plans call for it to provide management for the on-site staff, and more significantly, to permit its faculty to play an active part in the work of the Toxic Hazards Research Unit. Two sets of resumes were submitted to the Sub-committee, one for the on-site team and the other for the University-wide Research Management Working Team. The latter is a group of about fifteen eminent scientists representing as many disciplines related to toxicology. It is hoped that this group will provide a stable source of qualified investigators to work in this important area. This might be achieved through both the ten percent of the budget that may be allocated to the University laboratories and by using faculty members in on-going Air Force research work whenever the opportunity arises. Their contribution could take the form of advice on program planning and review, actual data generation, evaluation, and interpretation, or collaboration in research. The Sub-committee thought such active contacts with the University of California faculty should help to overcome a possible trend toward intellectual and professional isolation by some of the staff of the Toxic Hazards Division. Certainly collaborative work would be beneficial to the younger AMRL staff, both military and civilian, and to students of toxicology of the University of California. The potential benefits of the relationship should be pursued aggressively by both parties.

B. Scientific Effort

1. Research Work to Date:

a. Description

AMRL was established in the 1950's. It was sharply upgraded in the early 1960's when it became apparent that the manned spacecraft programs called for toxicologic information that was not available. Lately, there has been a diminished need for information related to the space program or high-altitude flight environments, but in its place has come an increased demand for information related to environmental and occupational exposures, i.e., there is a need to assess the hazards that Air Force materials present to ground crews, to military and civilian workers at air bases, and to the public. In some cases the need for the new information has been mandated by the Environmental Protection Agency or the Occupational Safety and Health Administration. In other cases, it has been generated by recognition on the part of the Air Force that it must be able to evaluate the environmental and safety impacts of its activities.

The results of the Laboratory's work are reported in Air Force technical publications, in toxicology and pharmacology journals, and at scientific meetings and symposia. A symposium on toxicology is held annually at the Laboratory. Scientists from all over the world are invited and come for discussion of the Laboratory's work and the way it relates to that of others. There is no classified work at the Laboratory and all results are available to those who can use them. A bibliography of reports issued by AMRL since 1957 (Appendix 6) includes 267 entries.

b. Comment

The record is clear that the unit has concentrated on studies directly related to Air Force aerospace-military activities. Most of its work has been on propellants, aircraft and space cabin atmospheres, and airborne fire extinguishants. It should be noted that the information gained from the high-altitude toxicity studies has been a significant contribution to the success of manned space flight, aiding in determining safe environmental flight conditions for astronauts. In the Sub-committee's view, the AMRL has been productive. The work consistently has been of high quality and the laboratories and the staff enjoy a good reputation among their colleagues. The annual symposium is known internationally and attracts toxicologists from all over the world. They point with justifiable pride to the steady stream of reports or publications that have come from the Laboratory - an average of better than twenty papers a year for the last decade.

The Sub-committee noted, however, that, after a peak in 1966, the rate of publication has declined. Although it is still acceptable, it is no longer outstanding. The Sub-committee also noted a preponderance of Air Force technical publications and only a few papers per year in refereed journals. The Sub-committee recognized that the basic task of the Laboratory calls for it to answer specific problems given to it by the Air Force and that technical reports are an appropriate way to respond, but the Sub-committee believes that the Laboratory's data are of interest to the general scientific community and that more should be published in

regular journals. The Sub-committee also believes that objective criticism by journal reviewers has a healthy influence on research programs, and research work should be subjected to this criticism whenever practical.

Regular peer review would be another healthy influence. The Sub-committee was told that there is a Scientific Advisory Committee to the Secretary of the Air Force and another to the Surgeon General, and that these conduct periodic reviews of AMRL's work, but it suspects that such high-level advisory groups are unlikely to involve themselves with the details that determine the quality of a research program. The University of California Scientific Management Team is charged with review of the projects performed and planned but these representatives of the contracting institution cannot be regarded as totally impartial. The Sub-committee recommends that an outside group of qualified scientists be asked to provide scientific review of the research on a regular basis. This would help ensure optimal utilization of personnel, facilities, and funds.

2. Research Present and Future

a. Description

AMRL classifies its research efforts into seven categories. This classification is somewhat arbitrary but is informative because the names of the categories and the work in them indicate the scope and purposes of the Laboratory. The categories and some of the major projects within each are:

- i. Characterization of Air Force materials. This includes studies of jet fuels, such as JP-4 and JP-9 and their additives, rocket propellants, such as hydrazine and deuterium fluoride, and miscellaneous materials such as photochemicals and flare residuals.
- ii. Determination of toxic hazards from aircraft interior combustion products and fire extinguishants. Among the first group are off-gasing products from polyurethane foams, potting compounds, and other materials used in aircraft. Among the second are the fluorocarbon fire extinguishants that are being introduced into aircraft and other Air Force and civilian installations. These data are needed to supplement the information available from the private sector for application to unique operating conditions in military aircraft and ground installations.
- iii. Development of occupational health standards for fuels, lubricants, materials, and chemicals. The subject materials are fuels, propellants, and miscellaneous materials used by the Air Force and to which ground personnel of the Air Force and its contractors are exposed. Many of the materials or conditions of exposure are unique to the Air Force.
- iv. Development of emergency and short-term exposure limits for rocket fuels, laser chemicals, and new Air Force chemicals. The subject materials are those of categories i and iii which are used in such quantities that an accident might release amounts sufficient to endanger crews or nearby persons.

The preceding four categories involve direct assessment of toxicity --- estimation of safe levels. Three of the four (i, iii, and iv) are the responsibility of the THRU contractor. The other is the responsibility of the Air Force laboratories. The following three categories are essentially supportive or supplementary to the direct assessment of toxicity.

- v. Investigation of the mechanisms of effects, treatment, and protection for new Air Force chemicals. In addition to fundamental knowledge on mechanisms, these studies are intended to provide information that will be beneficial in the diagnosis and treatment of toxicity that may occur upon exposure.
- vi. Identification and characterization of environmentally hazardous materials. In some cases the materials under investigation in the Laboratory are ill-defined mixtures and the definition of their toxicology depends on establishing their composition. In other cases it is the combustion products that are toxic, and these must be identified before they can be studied. Thus this category includes efforts at chemical analysis and identification.
- vii. Development of environmental quality criteria for Air Force operations. The Air Force is required to file environmental-impact statements with the Environmental Protection Agency. It is also responsible for the effects of accidental spills. This category includes attempts to assess these problems and to establish tolerance limits.

The Laboratory employs a number of techniques in the course of its work. It determines LD₅₀'s after oral and intraperitoneal administration of materials to mice and rats. It also determines LC₅₀'s during exposure of mice and rats to vapors and gases. Eye- and skin-irritation assessments are made on rabbits and guinea pigs. The procedures are standard in laboratories throughout the world. Similarly tissues from the animals used in these studies are subjected to gross and microscopic examination according to standard procedures.

The Laboratory has two kinds of exposure chambers for more extensive investigation of compounds of particular interest. It has a number of the "Rochester" chambers, which are used by a number of laboratories. It also has the "Thomas Domes," which are unique to this facility. These are described in more detail below; they are large chambers capable of holding several species of animals simultaneously. They are equipped with elaborate atmosphere-control systems and chemical-monitoring devices. They are also equipped for electronic monitoring of the test subjects. Although ordinarily used for animals, they may be used for human exposures when that is appropriate.

The Laboratory has veterinary pathologists and other personnel and equipment appropriate for histopathologic and clinical chemistry studies. Electron microscopy is also available. Most of the pathology is done at the Laboratory but a sizable part of the histopathology is sub-contracted to a commercial laboratory in St. Louis.

In addition to direct toxicologic assessment, the Laboratory conducts fundamental research in areas in which it hopes to advance technology or to understand the mechanisms of toxic materials. At present it is studying techniques of analytic chemistry and the physiologic mechanisms and changes in cellular ultrastructure that may explain the toxicity of certain agents. It also is trying to develop new and better models for toxic evaluation. The last has two facets: (1) studies to identify the animal species best suited for extrapolation of experimental findings to man, (2) studies seeking the time, dose, and route of exposure that will provide the most reliable information in the least possible time. The Laboratory is also investigating carcinogenesis and mutagenesis.

b. Comment

The number of investigations being conducted at the Laboratories was too large for the Sub-committee to investigate each. Instead, it requested and received written descriptions of all projects (listed in Appendix 6) and verbal presentations on major and representative projects currently under way. Included among the latter were:

Jet Fuels. In spite of the huge amounts of these materials that are used throughout the world, little is known about their toxic hazard. The Laboratory is beginning an investigation of the potential toxicity of JP-4 and JP-9, which in this country are used exclusively by military aircraft as fuels.

Fluomine. An unusual chemical being investigated as a possible component in a novel breathing oxygen supply system for ultra-high-altitude military aircraft.

MISCH Metals. Mixtures of rare earth and other metals used in flares. Their combustion products land on test ranges and pose a potential threat to personnel and animals in the area and possibly to ground water from the ranges.

Fluorocarbon fire extinguishants. Materials that are revolutionizing fire fighting. They are to be added to the atmosphere automatically and in high concentration as soon as a flame is detected. Their superiority as fire suppressants is unquestioned but they cannot be used until their safety for personnel is demonstrated unequivocally. Although initial use will be in military equipment, they have great potential for civilian applications.

Coal tar volatiles. A project to assess the toxic hazard to workmen in plants that produce coal tar. Only indirectly of interest to the Air Force, the project is supported by a contract from the National Institute for Occupational Safety and Health (NIOSH).

Fuel Additives. The additives being studied now are a group of amines that act as metal scavengers for engine protection.

Triphenylstibine. A photochemical developer used in reconnaissance.

Deuterium fluoride. An exotic material being considered as a high-thrust propellant for rockets.

Methylene chloride and methyl chloroform. Halogenated hydrocarbons used by Air Force personnel for de-greasing. They also are used as solvents in plastics and adhesives used in construction of equipment. They slowly volatilize from the latter and contaminate the environment in which the equipment is placed.

Monomethylhydrazine. A rocket fuel.

The procedure for choosing agents for study and assigning priorities is complicated, but the result appears to be on target. The material presented to the Sub-committee indicates that the major effort will be evaluation of hazards from rocket propellants, high-energy fuels, oxidizers, rocket and jet fuels and additives, fire extinguishants, and environmental pollutants. These are obviously relevant and responsive to Air Force needs and responsibilities, and clearly in support of Air Force activities. The jet fuels being investigated are used only by military aircraft and the Air Force is the sole or major user of fluomine, deuterium fluoride, and monomethylhydrazine. Although other agencies, military and civilian, will use the fluorocarbon fire extinguishants, it is necessary for the Air Force to know the effects of these materials in the special circumstances of flight crews. Similarly, other agencies use chlorinated hydrocarbon solvents but not commonly in the ways in which the Air Force uses them.

The Air Force need for information about coal-tar volatiles was more tenuous. Although the information was said to be valuable to some suppliers of Air Force needs, the project clearly was being run as a courtesy to another government agency and as a way of using exposure chambers that otherwise might have been idle. Similar arrangements with the National Aeronautics and Space Administration, the Navy, and the Department of Transportation have existed in the past. The Sub-committee is of the opinion that this kind of cooperation is useful so long as it does not detract from the primary mission to support the Air Force.

It is quite proper that a national resource such as AMRL should be available to the nation without unduly limiting its availability for Air Force needs. Present policy limits non-Air Force-related activities to a maximum of 20 percent at any one time. The Sub-committee approves of this policy.

The Sub-committee examined the procedure whereby protocols are designed and approved and was satisfied with these. The experiments seemed to be carefully designed and planned, with simple, inexpensive tests being conducted first and the need for more complicated or expensive ones being evaluated before they are undertaken. The techniques and procedures generally are those used in reputable laboratories throughout the country.

Three specific projects were described in detail as representative of work done in major components of the Laboratory:

1) Acute toxicity studies. These are the bread and butter work, and a number of such projects are done each year. AMRL, like all other toxicology laboratories, uses animals for the evaluation of chemicals to which people may be exposed. In the Sub-committee's opinion such toxicology studies in animals provides the best basis for conservative judgment in establishing safe conditions for human exposures. The only alternative is experimental exposure of humans.

Several species of rodents and non-rodents are used routinely; mice, rats, dogs, or monkeys most commonly. At the termination of the study, all animals are euthanized by appropriate methods for the essential anatomical studies. Both the animal work and the pathology seemed to be in competent hands and the Sub-committee had no recommendations to make. The only aspect of it that seemed unclear was the work being done by contract to the commercial laboratory in St. Louis. The staff at AMRL seemed convinced that excellent service was being received and the Sub-committee had no reason to doubt this. On the other hand, it knows that there are advantages in having close liaison between the toxicologist conducting the study and the pathologist interpreting the specimens and it thinks this might be difficult to arrange over this distance, particularly since the contract is too small (\$10,000 per year) to justify regular meetings between personnel.

ii) Toxicity of jet fuels. This study will be the major inhalation exposure project this fiscal year. It was scheduled after a review of published reports failed to reveal any long-term inhalation studies on gasoline, kerosene, or jet fuels. Since these materials are handled in huge amounts by Air Force personnel, it was thought necessary to obtain data that would make it possible to establish the safety of those who work in atmospheres contaminated with jet fuels.

The protocol calls for four animal species to be used - mice, rats, monkeys, and dogs. The exposure will be in the "Thomas Domes" and will continue for six months. Four domes will be used, each with a different environment. All four species of animals will be present continuously in each dome. In the first, the animals will receive filtered air and will serve as controls. In the second, the animals will be exposed to 25 parts per million of benzene in air. This is the Threshold Limit Value (TLV) for occupational exposures, i.e., it is the time-weighted average concentration deemed safe for employees to breath eight hours per day, five days per week during their working lives. Benzene was chosen because it is a major component of jet fuels and it may be necessary to distinguish between intoxication due to benzene and that due to other components of the mixture. The other two chambers will contain two different concentrations of jet fuel. Since the experiment is being done to establish an Approximate Threshold Limit Value (ATLV) for jet fuels, both concentrations are low and are expected to produce minimal or no intoxication of the animals.

The condition and behavior of the animals will be monitored continuously through the transparent walls of the chamber and periodically by technicians who enter the chambers. In addition, blood will be drawn periodically from the dogs and monkeys and sent to the laboratory for measurement of a number of basic constituents. If any animal should die during the experiment, it will be autopsied and its tissues examined carefully to determine the cause of death. Animals that complete the experiment will be sacrificed by humane means and their tissues will be examined for changes that might indicate subtle toxic effects of the exposure.

The Sub-committee had several comments about this experiment. First, they believed that it was necessary and, indeed, long overdue. There is little excuse for exposing large numbers of air or ground personnel to such common materials as fuels without some information on the potential hazard of such exposure. Air

pollution by these fuels creates a potential public health problem and adequate protection of people demands accurate information as to the amount of hazard, if any, they face. Furthermore, it is determined that, if there is a hazard, systems for handling jet fuels must be engineered so as to minimize human exposure. This cannot be done without accurate information on design targets.

The Sub-committee agreed that the "Thomas Domes" provide an excellent facility for this kind of experiment. Although this test will not use the maximum capabilities of the domes, the fact that they are big enough to hold large numbers of several species simultaneously, and that atmospheric conditions can be carefully controlled and monitored, makes them unusually valuable for studies of this kind. In addition, the ease with which they may be kept clean and sanitary, and with which animals can be cared for during experiments, contributes significantly to studies conducted in them.

The Sub-committee found no reason to fault the choice of animals for the study. Mice and rats are standard in toxicologic research and a great deal of information can be gained from them. On the other hand, results obtained from them sometimes are difficult to extrapolate to man and good current practice calls for one or two additional nonrodent mammalian species to be used. In practice, the available alternatives are primates, dogs, and cats; other domesticated animals (including the so-called miniature swine) are too large to be used practically. Dogs are most often used. Cats are not suitable because their practice of grooming their fur causes them to ingest large amounts of material and thereby confound attempts to interpret the inhalation toxicity of materials. Primates may seem to be ideal, but their biochemical resemblance to humans is not as close as their appearance. Furthermore, they are difficult to handle; they are vicious and may suffer from tuberculosis, which they can catch from or pass to their handlers, and which may modify their experimental pulmonary pathology. In addition, since they are difficult to breed successfully in captivity, the use of these animals is putting heavy pressure on wild populations and threatening to extinguish some. A national effort should be mounted to create an adequate, domestic laboratory-bred supply of primates, but until that is accomplished the threat of endangering species is sufficient to justify the use of dogs.

While in agreement with the purposes and design of the experiment, the Sub-committee noted some details that seemed to have escaped the attention of the investigators. Although not critical to the outcome of the experiment, closer attention to these would be appropriate. One of the problems of working with jet fuels is that they are not defined chemically. They are formulated by a number of petroleum companies to performance specifications and differ greatly from one batch to another, depending on source and availability of raw materials and time of manufacture. These characteristics make it difficult to do precise toxicologic evaluation of them. The staff of the Laboratory recognizes this difficulty, and plans to deal with it by using a single batch of material for its entire study.

The Sub-committee suggests that more extensive chemical analyses of this and other batches of jet fuel would provide a firmer base for extrapolating toxicity data to jet fuels generally. This batch is already purchased and stored

on the Base. Furthermore, the staff pointed out that the range of toxicity of the various materials that can be put into jet fuels is not so great as to produce major differences among batches. This may be true but the Sub-committee would feel more comfortable if the Laboratory had plans to analyze the material for important parameters such as the benzene content. The Sub-committee also was surprised to learn that detailed chemical monitoring of the environment was not planned. The staff believes the parameters desired can be obtained without the expense of monitoring. The Sub-committee believes that good chemical data should be obtained using the sophisticated chemistry facility available. It also notes that the plans call for the fuel to be vaporized by a bubbler system, which will in effect cause a fractional distillation. While this may simulate the reality of fuel-exposure conditions, the Sub-committee believes that it reinforces the comments on the need for a careful and detailed chemical analyses initially with subsequent routine analysis of indicator components.

In passing, the Sub-committee notes that similar comments might be directed toward other projects conducted in the Laboratory - for example, the current study of methyl chloroform. The material being added to the air in the domes is a commercial grade containing significant amounts of impurities and additives, some of which might be toxic in their own right.

iii) Toxicity of low-molecular-weight fluorocarbons. This group of projects was representative of the fundamental research at the Laboratory. An extensive effort is under way to determine the mechanism of toxicity of low-molecular-weight fluorocarbons, particularly CF_3Br , which are being proposed for fire suppressants in military and civilian situations. The effort is justified on the grounds of immense potential use of these materials and the possible exposure of large numbers of military and civilian personnel. The Laboratory has recently completed a series of investigations of the effects of the material on animals and human volunteers, and these data have contributed significantly to the design of the fire-suppressing systems. The Laboratory now is interested in detecting subtle toxic effects that might have gone unnoticed in the initial work, and to investigating the mechanism of toxic effects that are seen at very high concentrations.

Several projects are under way or contemplated. The first is directed at the effects of fluorocarbons on the cardiovascular and autonomic nervous systems. Very high concentrations of these materials induce an acute drop in blood pressure. They also interact with catecholamines to produce acute lethal ventricular fibrillation. These effects are being studied in anesthetized dogs and in vitro systems such as the Langendorf model. Another project studies the effect of the fluorocarbons on drug-metabolizing enzymes and on mitochondrial function. In a related study, organs, particularly hearts, are being examined by light and electron microscopy to determine what effects, if any, the fluorocarbons have on ultrastructure.

This group of experiments apparently constitutes the principal effort at fundamental research in the Laboratory. The Sub-committee is wholeheartedly in agreement with the attempt to understand mechanisms and it, in principle, strongly endorses the notion that the Laboratory should be engaged in research on mechanisms

of toxicity. However, it was surprised at the concentration of effort on this one compound. The problem of cardiac arrhythmias is important but the Sub-committee could not be certain that understanding had ripened to the point where the problem required the extensive instrumentation that was being employed. The rationale for the electron microscopy of cardiac tissues during the search for the cause of catecholamine-induced ventricular fibrillation was not completely clear. The rationale for the study of hepatic function, i.e., that these materials are related to halothane, a known hepatotoxin, was sounder but still seemed too weak to justify the extent of the effort being expended.

While these comments were raised with regard to this specific group of projects, it was not clear that the investigator himself was responsible for the faults. Instead, only two scientists seemed to be interested in this kind of work and their enthusiasm for it seemingly had attracted collaboration and support out of proportion to the project's significance. Thus, the difficulties seemed to be more asymptomatic of the broader problems that will be discussed below than inherent in either the projects or the investigators.

The Sub-committee offers the following summary comments about the research program.

The materials chosen for investigation are reasonable for an Air Force laboratory. The emphasis is on hazards and environmental problems directly related to Air Force activities. Furthermore, most of the studies are of acute or relatively short-term exposures, the kind most likely to be encountered by Air Force personnel. The recent efforts to include more chronic studies are needed to assess the influence of Air Force activities on the environment and to meet the requirements of various federal laws governing environmental impact. Some of this new work, such as the exposure to jet fuels, is highly relevant to Air Force needs. Other parts of it, such as coal-tar volatiles project, are less so and are appropriately supported by non-Air Force funds.

The Sub-committee found the staff to be experienced, knowledgeable, and well qualified to conduct toxicologic research. Their interest focuses on traditional methods in which gross and microscopic examination of tissues are supplemented by established methods of analyzing blood and other body fluids. This work seemed competently done.

Thus, the Sub-committee was satisfied with what it saw in the main thrust of the laboratories. To be sure, they found details to criticize, but these are probably not greater than could be found in any laboratory subject to such an inspection.

The principal questions that came to the Sub-committee's mind were as much philosophic as scientific. That is, how much beyond histopathology is desirable in a modern toxicology research laboratory? The Sub-committee does not pretend to know the answer, but it notes that the question has not been adequately resolved at AMRL. The Air Force states that it needs the capability to do toxicologic research and its justification for this statement is sound. At the same time, it apparently has not made a full evaluation of what it needs or a full commitment to the facility that it constructed to do the work. Accordingly, the projects being assigned to AMRL are inadequate in quantity or complexity to challenge the capabilities of the unit.

AMRL is based in a physical plant that contains many special facilities for atmosphere control, for chemical monitoring of atmospheres, for electronic monitoring of animals (or human volunteers) during and after exposure and for related chemical, pathologic, and physiologic research. It clearly is equipped for very sophisticated research but the projects under way do not use the sophistication that can be provided. Similarly, the staff is knowledgeable and experienced in conventional histopathology but in other areas is too small to fully use the research material present in the exposure chambers and spread more thinly over the various disciplines than optimal for productivity in any of them. Similarly, there is only a minimal effort to collect data outside the realm of the morphologist. The chambers and supporting laboratories are equipped and adapted for monitoring of physiologic and behavioral functions but these facilities are being used minimally, if at all. It has been noted that the effort to study basic mechanisms seems to be centered around one compound and in one unit of the Laboratory.

There seems to be a problem of indecision deriving from a lack of long-range goals and a commitment to them. There are several laboratories with unused equipment. The Air Force would do well to sharpen its objectives in toxicology by carefully evaluating the potential present at AMRL and take steps to develop and use it to meet the growing needs for toxicology research. Top-level management needs to give more consideration to planning long-range goals for AMRL in order to avoid responding excessively to expediences of annual budgets.

3. Advisory Function

When toxicologic questions arise from the Air Force or its contractors, the staff of the Toxic Hazards Division gives advice and sets unofficial limits on the use of hazardous materials. These suggested limits, though without official status, govern practice within the Air Force and its contracting industries until replaced by more definitive information. This is an indispensable service, but it seemed distressingly informal. The senior scientists who are responsible for replying to such queries are men of great experience, are very knowledgeable in their areas, and have the necessary contacts to obtain information that they may not have at their fingertips, but successful operation of the advisory function depends on the availability of them and their experience. There should be a system for providing data when these individuals are not available. The Sub-committee was appalled at the virtual absence of library facilities to provide reference material that might be needed for the advisory function or for more detailed information than individuals can possess. The Sub-committee is not critical of the people involved; they seem to have functioned well in this task, but it feels that they ought to be backed up by appropriate files and library facilities.

4. Physical Facilities

The physical facilities are quite impressive and compare favorably with research laboratories elsewhere in the United States. The laboratories are clean and well kept. The chemical and hematologic equipment and the autopsies and tissue

processing facilities are entirely satisfactory. No purpose would be served in attempting to take note of all the equipment seen, but in general the laboratories seemed very well equipped to perform analytical chemistry, electron microscopy, pathology, clinical chemistry, surgery, and physiologic and other studies. The Sub-committee looked closely only at those facilities needed for the primary programs of the Laboratory.

a. Analytical Facilities

A perusal of the list of major equipment furnished to the Sub-committee shows that the Laboratory is well equipped by current standards to perform a wide variety of complex analyses. One of the most impressive instruments is the recently acquired DuPont thermogravimetric analysis/mass spectrometer. The auxiliary reference-data component of this system makes it possible for AMRL to analyze small samples of complex substances rapidly and accurately. Although not all the instrumentation is as modern, it is our judgment that, with the possible exception of trace metal analyses, the Laboratory is well equipped to carry out its assigned missions.

b. Toxicology Facilities

The exposure facilities, consisting primarily of the "Thomas Domes" and attendant service facilities, are some of the finest animal-exposure facilities to be found anywhere.

The "Thomas Domes" are elaborate hemispherical structures designed and constructed to permit research at reduced pressure, thereby allowing inhalation studies in atmospheres simulating those encountered in actual flight or emergency conditions. They are equipped with highly sophisticated monitoring and atmosphere-generating and control equipment. Air locks both from the floor below and from the side permit access for personnel, animals, and equipment without interrupting experiments. These domes, constructed at a cost of several million dollars, have received much publicity and are regarded by many as a unique national resource. The present research programs of AMRL do not call for reduced-pressure studies, hence many of the design features are not being used. Certainly elaborate chambers of this type would not be constructed for ordinary exposures at atmospheric pressure, but the present chambers ought to be kept in good working condition for future needs, and, in addition to the value of the research itself, the work being done in them is a practical means of keeping the units operational.

In addition to the "Thomas Domes," there are numerous chambers of different design, which give the laboratory an overall capability for inhalation research sufficient to rank it among the top laboratories in this field. The remaining entities within the Division are standard toxicology-research facilities and are adequate for the requirements of the work. Improvements that should be considered include filter tops for rodent units, mass air-flow cabinets, rooms, or tents to minimize contamination and improve animal quality prior to assignment to specific research programs. Additionally, the animal-support facilities within the Toxic Hazards Division should be enlarged to meet the anticipated expansion of projects requiring long-term maintenance of animals. The use of mobile trailers, as

currently contemplated, can serve only as a temporary answer. In summary, the facilities and equipment available are modern, well designed, and capable of meeting the requirements of this research program.

5. Animals for Research

a. General

The Veterinary Medicine Division is administratively independent of the other four Divisions and reports directly to the Commander of AMRL. Under AMRL Regulation No. 163, the Chief of the Division is "charged with the responsibility for the supervision, management, and operation of the experimental animal program." He is further responsible for operating the Animal Care Section and for providing animal-care support to research activities in the other Divisions. Copies of these regulations are included in Appendix 8. In addition to specific policy statements on animal-care practices, the regulations require conformance to the standards of the Guide for Laboratory Animal Facilities and Care, first published in 1963 and revised in 1965, 1968, and 1972 by the National Academy of Sciences-National Research Council, and to the regulations and standards of the Department of Agriculture under Public Law 89-544 Laboratory Animal Welfare Act as amended by 91-579.

i. Procurement

In general, procurement follows recommendations of the Institute of Laboratory Animal Resources of the National Research Council. Specification is the responsibility of the Chief of the Veterinary Medicine Division, and procurement of all animals, regardless of species, is under administrative control of the animal-research facility. Requirements or limitations, evaluation of suppliers, selection of suppliers, and receipt and delivery of animals are the responsibility of this office. Orders and contracts are handled through normal Air Force procurement procedures.

A quality-control program, described in Appendix 9, assures the health of incoming animals. Depending upon the species, the program may include screening for internal and external parasites, hematology, clinical chemistries, and serologic monitoring. These procedures are handled by the Pathology Branch of the Toxic Hazards Division. Additional limited laboratory capabilities are available within the Vivarium. Serological screening for specific viral antigens is obtained, when needed, by submitting samples to a commercial testing laboratory for murine viral screening. Together these laboratory capabilities are sufficient to meet the Division's requirements.

The Sub-committee judged the animal-procurement system to be adequate but perhaps unduly restrictive. It is not always logical to purchase on the basis of bids for animals, since the quality of the animal is more important than the cost and the Air Force should be able to use special sources when necessary. It would be much more appropriate to develop a reliable source and continue obtaining animals from that source so that the background of the animal or group of animals

and the source itself can become well known to the toxicologist and pathologist. In essence, it might be better to set up a 5-to-10-year contract with a supplier. The contract should contain a clause permitting termination should the quality of the animals deteriorate. It is suggested that the Air Force consider adopting the animal-procurement procedures in use at the National Institutes of Health.

ii. Care

Upon receipt by the AMRL, animals are put under the care of a Doctor of Veterinary Medicine and are placed in quarantine for preliminary observation. The pens or cages are adequate in size and the rooms are clean and air-conditioned. The animals are examined for parasites and various diagnostic tests are done to ensure that they are healthy. After the observation and conditioning period, the animals are moved to another building where they are kept in adequate cages in air-conditioned, clean rooms. All holding quarters meet or exceed the requirements of the Department of Agriculture and the local authorities.

The care of all animals appears to be excellent. At the present time there are two veterinarians; a third position is temporarily vacant. Of the present personnel, one is Board Certified in Veterinary Surgery and the other in Laboratory Animal Medicine. The vacant position probably will be filled by someone with Board Certification in Laboratory Animal Medicine. Additionally, the facility has ten technicians who are certified by the American Association for Laboratory Animal Science (AALAS). At least one is certified as a Laboratory Animal Technologist, the most advanced rating given by AALAS. Procedures for care are excellent and meet or exceed those in existence at other facilities in this country.

Animals transferred to the Toxic Hazards Division are cared for by the contractor, but he must meet the standards established by the Chief of the Veterinary Medicine Division. Direct responsibility for assuring the proper use and care of all animals is retained by the Chief of the Veterinary Medicine Division. The care provided to these animals appeared entirely satisfactory, although the facilities are more crowded than those in the Vivarium.

b. Use

i. Description

Written AMRL regulations (Appendix 8) require all protocols involving animals to be reviewed and approved by the Chief of the Veterinary Medicine Division. This review includes selection of proper animal models, evaluation of procedures to prevent any unnecessary pain or stress and compliance with guidelines established by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and the regulations of the U.S. Department of Agriculture and Air Force. AMRL was the first facility in DOD to be accredited by AAALAC.

The selection of species is a function of specific studies including general considerations of anatomy, physiology, and appropriateness as a model. Specific selection of a given species or strain is, therefore, based upon many factors and

the final decision rests with the senior investigator after consultation with the Veterinary Medicine Division. Most of the research, particularly the preliminary acute phases, is conducted on rodents. Occasionally, the anticipated circumstances of human exposure to a given chemical require more refined data and this requires additional sub-chronic or chronic studies in one or more non-rodent species. Economics and existing scientific data often dictate the use of dogs and/or primates.

ii. Sub-committee Assessment

The procedures followed in the selection and use of animals in specific research programs are such as to assure the humane use of animals and the development of meaningful data. Proper controls are exercised so that individual investigators are not making decisions without input and guidance from appropriate personnel. These procedures meet or exceed in quality those in biomedical programs throughout the country and are in full compliance with standards established by Federal law, Air Force regulations and the AAALAC.

c. Use of Beagles

i. Description

In fiscal year 1973, approximately 172 Beagles were used in chronic and short-term studies. Two hundred Beagle dogs have been ordered for fiscal year 1974. About 35 will be anesthetized and used for acute studies. They will not be permitted to regain consciousness and euthanasia will be accomplished at the end of the experiments. The remainder will be used in chronic inhalation studies, about one half for jet-fuel studies, as described above, and one half to test the safety of fluomine that may contaminate aviators' breathing oxygen. The animals will be exposed to concentrations selected to produce no effects or minimal and reversible effects. About one quarter will be controls and exposed only to air. Thus, there is no intent to produce serious injury to the animals and there should be no pain. Laboratory tests (withdrawal of samples of blood) will be done periodically during exposure and anatomical studies will be done at the termination of the experiment. The animals are subjected to euthanasia by humane procedures, usually the intravenous injection of a barbiturate.

ii. Sub-committee Assessment

The Sub-committee conducted extensive discussions with the AMRL staff as well as among themselves on the choice of species for the acute and chronic studies. There are only three species of non-rodent mammals that are large enough for complete and accurate chemical and histopathologic observations, and for which there is adequate background knowledge of their physiology, biochemistry, anatomy, and response to toxic stress; these are monkeys, cats, and dogs.

In the experimental use of animals to add to our knowledge of reactions to conditions of all kinds, it is of the greatest importance to use animals that give the most dependable experimental results. This is especially true

when the end purpose of the experimentation is to provide data relevant to the activities and well-being of human beings. This is certainly the case with the experimental activities of immediate concern here.

The scientific rationale for the use of Beagle dogs in toxicologic research rests on many points including the following:

(a) The variations between genera and between species of mammals, including man, make it imperative to utilize more than one species in predicting the toxicity of chemicals to man. A classic example of this requirement is the thalidomide experience, in which rats and mice did not show the effects observed in man and later found in other test species.

(b) The predictive quality of toxicological research improves with the accumulation of knowledge on the comparative physiology, biochemistry, anatomy, and other relevant qualities of any given test species in relation to man. The decades of investigations with dogs, especially Beagles, provides a unique backdrop of such information. Dogs closely resemble man in many ways. Anatomically dogs, like man, are monogastric, their cardiovascular and hematologic systems are comparable to those of man, and many of their immunologic mechanisms are similar to man's.

(c) Mongrel dogs are useful for certain very elementary short-term studies but are totally unsuitable for the high quality of research needed for predicting human effects from chemicals, for example, long-term exposures. Mongrels are usually infested with parasites, and often are diseased and in poor health. Purebred dogs, especially Beagles specifically developed and bred for research purposes, do not have these problems and are less likely to die of extraneous causes during experiments. Thus, an experiment with purebred Beagles requires many fewer animals - perhaps only one tenth as many - to get statistically significant results.

(d) Although other species are indeed useful and required in toxicological research, none of the available species can replace the Beagle dog. The miniature pig was considered as a possible non-rodent mammal, but it is too new and it will take several years to generate the necessary background of information for valid comparative purposes. Furthermore, while the miniature pig is smaller than swine raised for meat production, it attains a weight of several hundred pounds, thus is hard to handle and requires large amounts of food and space. Primates are in scarce supply from the importing sources and are becoming endangered species. U.S. breeding programs for primates will not be effective for many years and probably never will attain a rate of production sufficient to replace dogs. For example, monkeys seldom produce more than one offspring at a time. For these and similar reasons, primates should be used only where they are essential. For example, the pathologist requires extensive data and experience on the normal variations found in tissues of any test animal. Such information is available for the Beagle. Cats differ significantly from man in their hematology although resembling man in other ways. Their habit of preening makes them poor candidates for inhalation exposures. There are very few sources of cats bred under controlled conditions.

The Sub-committee concluded that, as a general principle, monkeys should only be used when their unique characteristics were vital to the research efforts. Monkeys are difficult to breed in captivity and indiscriminate use of them will put an excessive drain on the wild populations and endanger the survival of the species. Cats are not useful for inhalation studies because they groom their fur and ingest any material on it. Therefore, it frequently is essential to use dogs as the non-rodent species. Dogs of unknown background and pedigree are usually of adequate quality for acute toxicity studies. However for reliable studies of physiology, pharmacology, or chronic toxicology, it is important to use dogs of as nearly uniform characteristics as possible. Purebred Beagle dogs are raised for these purposes. They are separate and distinct from the pedigreed dogs raised for show, hunting, or as pets.

Beagles have one characteristic that can be disadvantageous, the volume and tonal qualities of their bark. A noise level of 105 db is often reached in the vivarium. The regulations of the Occupational Safety and Health Administration limit human exposure to this level in order to prevent hearing loss, and this amount of noise during an experiment can significantly alter the results from the dogs themselves and other animals in the vicinity; this applies especially to the behavioral responses of monkeys. Accordingly, under some laboratory conditions, it is necessary to reduce the volume or intensity of the dogs' bark and to modify its tone. The term "debarking" is a misnomer sometimes applied to the simple surgical procedure conducted under anesthesia to remove a small piece of a dog's vocal flap. Upon recovery from the anesthetic, the dog is entirely capable of communication and self-expression. There is regrowth of the removed tissue and restoration of the bark in a relatively short time. A better term for this procedure is "voice modification."

The Sub-committee understands that the present procurement requirement is a trial aimed at reducing the noise problem and may not be a continuing or repeated requirement. Although voice modification is a well standardized, frequently used procedure that can be performed humanely, the Sub-committee believes that it should not be a routine, automatic procedure for all dogs entering the laboratory. The Sub-committee suggests that policies and criteria be developed for determining which experimental programs require voice modification and which do not. The control and conduct of such operations should be the responsibility of the Veterinary Medical Division.

Although no animal is a perfect model for man, the use of a combination of species can provide a basis for extrapolating toxicity studies to anticipate safe exposure conditions for man. The Beagle dog is a necessary component of that combination and cannot be adequately replaced at this time or in the near future.

Committee on Toxicology

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Herbert E. Stokinger, Ph.D., Chief, Toxicology Branch, Division of Laboratories
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Sub-committee to Review WPAFB Toxicology Program

- Frank G. Standaert, M. D., Chairman, Department of Pharmacology, Georgetown University School of Medicine, 3800 Reservoir Road, Washington, D. C. 20007
- H. W. Gerarde, M. D., Ph. D., Professor, Fairleigh Dickinson University, Medical Director, Becton, Dickinson, and Company, Rutherford, New Jersey
- Lloyd W. Hazleton, Ph. D. Retired. Founder of Hazleton Laboratories, 9200 Leesburg Pike, Vienna, Virginia 22180
- Alexander Leaf, M. D., Chief of Medical Service, Massachusetts General Hospital, Boston, Massachusetts 02114
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- Harold M. Peck, M. D., Executive Director of Safety Assessment, Merck Institute for Therapeutic Research, West Point, Pennsylvania 19486
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- Joseph F. Borzelleca, Ph. D., Independent Reviewer, President of the Society of Toxicology, Professor of Pharmacology, Health Sciences Division, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia 23219
- Donald D. McCollister, Independent Reviewer, Ag-Organics Department, Dow Chemical Company, P. O. Box 1706, Midland, Michigan 48640
- Carrol Weil, Independent Reviewer, Past-President of the Society of Toxicology, Carnegie-Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213
- Ralph C. Wands, Staff Officer, Advisory Center on Toxicology, National Academy of Sciences, 2101 Constitution Avenue, Washington, D. C. 20418

res. Palo Alto, CA. Information pur- (P164)

Undersea Center, 3263 E. Foothill Pasadena, CA 91107.

PUTER PROGRAM FOR O-TYPE ELEC- WITH GRI: INCLUDED, one each- PROGRAM FOR SMALL SIGNAL GAIN CALCULATIONS on traveling wave one each—FOB Crane Indiana. Delivery and implementation within days after date of contract. Inspection at destination—IFB N00164- Bid Opening 27 Jun 73. Request bid (P165)

ing Officer, Naval Ammunition Crane, IN

ENERATORS, Bit Anomalies, Pulse Generators, and Pulse Time Delays mfg by Honeywell, Inc., 2 each Delivery to Fort Monmouth, NJ. RFP (P163) — RFP due date 27 Jun 73. See Notes 40 and 73. (P163)

Fort Monmouth Procurement Branch and Production Directorate States Army Electronics Command MODEL-PP-CM-GP, Fort Monmouth NJ 07703

Supplies and Devices.

Notice. CARDS, MENU, IBM, Items Total of 1,740 Mx. Delivery to Army Officer, AFM 2847, Bldg., 3450, Ft. TX 78236. Solicitation F41615-73- being issued approx., 20 Jun 73.

Procurement Division (LGPS), Lackland TX 78236

Maps, and Public Publications.

DESCRIPTIONS, MAGAZINES AND PER- term contract for period 9-1-73 thru definite quantities—for delivery to Reg. Office—Bid Opening 20 Jun 73.

Business Service Center 909 First Ave., 1009, Seattle, WA 98104

OKLET TITLE: Caution: Asbestos Dust, — RFP 39 — RFP due date 28 Jun 73

PHS/MSMHA/National Institute for Personal Safety and Health, 3235, Cincinnati OH 45201

Paints, Sealers, and Adhesives.

MEL, ALKYD, LUSTRELESS, Fed Spec Color MIL-P-13240B — 6010-NSN Field Drab 2335 gal. color 30277 Sand 37039 Black 375 gal — PRE-Coating, Canvas, Fed Spec TT-P- MIL-P-13240B — 8010-NSN color 37038 color 34379 Forest Green 410 gal. Field Drab 410 gal. color 30277 Sand Delivery to Fort Hood, TX by 15 Sep 73 — IFB DAAK02-73-B-2357 — Bid Jun 73. Telegraphic Bids must include unit prices, time and delivery all other info required by bid. Bidder that bidder agrees to all terms, and provisions of IFB. Call Mrs. Melchior on 703 664-5748. (P165)

TY, GASOLINE, WATER THINNABLE (See Use) to meet requirements of Purchase Description which will be Attachment No. 1 to IFB. Colors to conform to color chip number of 55 — colors and qty to be furnished: 34379 Forest Green 1,490 gal. 573 gal. 30730 Black 560 gal.; 34102 Dark Green 600 gal.; Green 300 gal. 34287 Olive Drab 300 gal. Brown 150 gal. 30257 Earth Yellow 21 Desert Sand 150 gal. 30217 — Deliveries to various U.S. locations within the continental United States IFB No DAAK02-73-B-2359 — later than 25 Jun 73. Telegraphic Bids authorized and must include items, prices, delivery schedule and all

info required by bid, with statement that bidder agrees to all terms, conditions and provisions of IFB. Call Mrs. Melchior or Mrs. Hopkins on 703 664-5748. (P165)

USAMERDC, R&D Procurement Office Fort Belvoir, VA 22060

81 Containers, Packaging and Packing Supplies

81 -- CYLINDER COMPRESSED GAS NITROGEN OIL FREE, FSN 8120-00-985-7275, IAW Fed Spec RR-C-901B dtd 1 Aug 67—1200 ea—Destins Tracy, CA and Richmond VA—IFB DSA-400-73-B-A338— Bid Opening 16 Jul 73. See Notes 72, 73 and 80. (P164)

Defense General Supply Center, Richmond, VA 23218.

81 -- COMMISSARY SUPPLIES, for a one (1) year period at McChord Air Force Base, WA and Fort Lewis, WA—IFB F45603-72-B-0490 — Approximate issue date on or about 27 Jun 73. See Note 56. (P165)

Base Procurement Office, P.O. Box 4178, McChord Air Force Base, WA 98438

81 -- AMENDMENT: — COMMISSARY OPERATING SUPPLIES, for Meat and Vegetable Depts— 17 Items—Requirements Type Contract period 1 Sep 73 through 31 Aug 74—Delivery to Norton AFB CA—IFB F04607-73-B-0328—Bid Opening 6 Aug 73. (P165)

Base Procurement Office Norton AFB CA 92490

81 -- PALLET, BOMB, UNIT LOAD ADAPTER, MK 75, MOD O, except as modified or amplified in IFB, Stock No. 81406715070 Deliveries to Mc Alester, OK—3,225 ea—IFB-N00104-73-B-1381 — Bid Opening 3 Jul 73. See Notes 2, 9, 45 and 64. (P165)

Navy Ships Parts Center, Mechanicsburg PA 17055

81 -- CONTAINERS, WITH LIDS, PAPER, PLAS- TIC COATED — Lot — IFB 13-R-APHIS-74Y — Bid opening 21 Jun 73 — Delivery to U. S. Dep of Agriculture, Plant Protection and Quarantine Programs, Phoenix AZ for the period from date of award thru 31 Dec 73. (P165)

U.S. Department of Agriculture, Animal and Plant Health Inspection Service, ASD, Administrative Operations Branch, 123 E. Grant St., Minneapolis, MN 55403

81 -- DRUM, SHEET STEEL, Type III, 55 gallon nominal capacity, new full removable head with gasket, Fed. Spec. PPP-D-711D dated 23 Jun 65 and Amendment No. 1 dated 13 Sept 66—6,500 each—IFB DAAA05-73-B-0124—Bid Opening 26 Jun 73. (P165)

Procurement Division, Attn: SMURM-L-P, Rocky Mountain Arsenal, Denver, CO 80220, Tel 303-283-0711, Ext 315

83 Textile, Leather, Furs, Apparel and Shoe Findings, Tents and Flaps.

83 -- CLOTH, DUCK, COTTON WARP AND RAYON FILLING, FSN 2205-151-6458 — MIL-C-43605 dtd 21 Oct 65 & Amd #1 dtd 16 Apr 71—1,475 yd—Dest Defense Depot Mechanicsburg, Mechanicsburg, PA—RFP DSA 100-73-R-1550 — Anticipated RFP issuance date on/about 22 Jun 1973. Solicitation time 20 days—All materials used in fabrication are to be furnished by the successful bidder (S)—See Notes 16 & 21. (P165)

83 -- PANEL MARKER, AERIAL LIAISON, Nylon laminated fluorescent 6 ft x 2 ft—FSN 8345-174-6645—MIL-P-40061B, dtd 12/31/70 and dwg 5-1-321, Rev 3 dtd 7/27/67—7,936 ea—Dest various U. S. defense depots—IFB DSA100-73-B-1547 — Bid issuance date on/about 14 Jun 73, 20 days adv.— See Notes 16, 19 & 21. (P165)

Defense Personnel Support Center, 2800 South 20th St., Philadelphia PA, 19101

84 Clothing, Individual Equipment, and Insignia.

84 -- KIT ASSEMBLY, Genlex Corp Part Number 70C2193-1 — 2018 ea—Dest various naval Air Stations—RFP DSA100-73-R-1552—Anticipated RFP issuance date on/about 15 Jun 73—All materials used in fabrication are to be furnished by the successful bidder(s)—See Note 21. (P165)

84 -- USERS, MAN'S ctn/poly twill tan shade 1505—FSN 8105-846-1849 series—MIL-T-41834C Type 1, Class 2 dtd 18 Aug 71 and Amend #1 dtd 19 Jan 72—91,003 pairs—Dest, Defense Depot Memphis, Memphis, TN—IFB DSA100-73-B-1553—Bid issuance date on/about 25 Jun 73. Solicitation Time, 30 days—The Government plans to furnish the following material: cloth twill cotton/polyester 6.3 oz max wt per square yards, AF, shade 15C5 tan type II 45" width—See Notes 16 & 21. (P165)

84 -- HELMET FLYING TYPE AFH-1, FSN 8415, IP/DES S-45-8 dated 15 Oct 1968 w/devs—930 ea —Dest Defense General Supply Center, Richmond, VA—IFB DSA100-73-B-1548 — Estimated issuance date 15 Jun 73. Acceptance time 20 days—The Government plans to furnish the following material: cloth, ballistic nylon weave 13.5 oz. min-15 oz. max P/sq yd. 47" width and 48" width; visor, polycarbonate, clear—See Note 21. (P165)

84 -- CHIN STRAP FOR PARACHUTISTS' HELMET, FSN 8470 — MIL-H-1988E—50,000 ea—Dest various, U. S. Defense depots and Defense General Supply Center, Richmond, VA—IFB DSA 100-73-B-1546—Bid issuance date on/about 13 Jun 73 10 days adv—The Government plans to furnish the following material: webbing 3/4" width—See Note 21. (P165)

Defense Personnel Support Center, 2800 South 20th St., Philadelphia PA, 19101

88 Live Animals.

88 -- LABORATORY ANIMALS — Solicitation 74-18—Bid Opening 27 Jun 73—Bid forms available 22 Jun 73, upon written request. (P165)

Veterans Administration Hospital University Drive C, Pittsburgh, PA 15240

88 -- DOGS, BEAGLE, Detarked, purebred six to nine months of age, est qty, 200 animals. Sex to be specified at time of delivery, will be approx half male, half female. Max orders, 50 animals, min. orders, 25, except by agreement. Delivery to be made direct to Laboratory on Wright-Patterson AFB by truck with no more than 12 hrs. travel time. Contractor must be licensed under provisions by PL-93-544 and the amendment included in the animal welfare act 1970 (PL-91-579), be in compliance with all federal, state and local laws pertaining to raising and transporting dogs and agree to inspection of his facilities prior to award and during effective period of contract as deemed necessary by personnel of Veterinary Med Div, 6370th AMRL or their authorized representative. Specific requirements must be met as to immunization, identification, size, uniformity of colony, animal housing, sanitation, veterinary care, records, temperament, and markings which will be specified out in the solicitation specification. See Notes 64 and 42 — IFB F33615-73-B-0685. (P165)

Procurement Division, Laboratory Support Branch, (PML), WPAFB, OH 45433

69 Subsistence.

69 -- CANNED, DARK, SWEET, CHERRIES, specifications, U. S. Standard for grades of cherries— 3440 cases of No 24 cans and 4,610 cases of No 6 cans—Destination, various—NIP DSA13M-73-E-04110 and Addendum No. 9—ADNIP closing date, 6 July 73. (P165)

69 -- COOKIE, MIX, OATMEAL — 7,600 cases— destination, various Conus Depots —NIP DSA13M-73-N-0463 and addendum No. 8—NIP closing date, 28 Jun 73. (P165)

69 -- LUNCHEON MEAT, Canned, specification, PP-L-00A30C—Destination, Alameda, CA—DSA 13M-73-N-0738—NIP closing date, 29 Jun 73. (P165)

69 -- JUICE, GRAPE, Canned, specification, Z-F 001742—11,610 cases—Destination, various—NIP DSA13M-73-N-0725 — NIP closing date, 27 Jun 73. (P165)

69 -- CHERRIES MARASCHINO, Specification, MIL-C-35071A—8,000 jars—Destination, various— IFB DSA13M-73-B-0754 — Bid Opening date, 3 July 1973—Proposed procurement is a 100 percent small business set-aside for items 1,2,3 only. (P165)

69 -- SAUCE FOR MEAT, Specification, MIL-S-35013B — 155,320 bt—Destination, various—IFB

HOME OFFICE:
600 MAIN STREET
RACINE, WISCONSIN 53403
414-832-8194

310 DODGE STREET
JANESVILLE, WISCONSIN 53548
609-732-9974

WASHINGTON OFFICE:
915 CANNON HOUSE OFFICE
BUILDING
305-225-3031

Congress of the United States
House of Representatives
Washington, D.C. 20515

July 5, 1973

The Honorable John McLucas
Acting Secretary of the Air Force
The Pentagon
Washington, D. C.

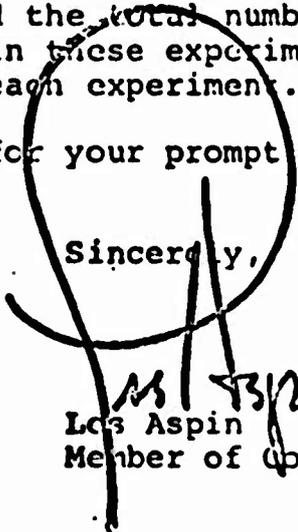
Dear Mr. McLucas:

It has come to my attention that the Air Force is seeking to buy 200 beagle puppies for experimentation at the Aerospace Medical Research Laboratory. Could you please inform me of the nature of these experiments and the specific need for dogs rather than some other animals in these experiments.

Also indicate the extent of all Air Force programs using animals and the total number of each kind of animal used in these experiments, as well as the nature of each experiment.

Thank you very much for your prompt attention to this matter.

Sincerely,


Les Aspin
Member of Congress

LA:mgt

JUDGE TONE

UNITED STATES DISTRICT COURT
FOR THE
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION - SEP 21 1973

THE NATIONAL ANTI-VIVISECTION SOCIETY, INC,
an Illinois not-for-profit corporation,
GEORGE J. TRAPP, CARL P. STILLMAN,
R. AGA., U.S.N. (Ret.), IOLA JUHL THELEN,
HELEN R. MILLER, LOUIS J. ROSKY,
VIRGINIA COLLETTE, DEBORAH FITZGERALD,
REV. MARK A. CANTREY, WILL RANFELLS,
LARRY ANDREWS, JULIA-JEAN STOKES, and
CHARLES A. GOULD, JR.,

Plaintiffs

-vs-

JAMES SCHLESSINGER, Secretary of the
Defense of the United States; JOHN L.
McLUCAS, Secretary of the Air Force of
the United States; GEN. IRBY B. JARVIS,
Commanding Officer of Wright-Patterson
Air Force Base; and LT. COL. JAMES H.
MORT, Officer-in-Charge of Aerospace
Medical Research Laboratory, Wright-
Patterson Air Force Base,

Defendants

CLERK
DISTRICT COURT

ADVISORY CENTER
ON TOXICOLOGY

SEP 7 1973

CIVIL ACTION

No.

730 2181

COMPLAINT FOR INJUNCTIVE RELIEF

NOW COME the plaintiffs. THE NATIONAL ANTI-VIVISECTION
SOCIETY, an Illinois not-for-profit corporation, GEORGE J. TRAPP,
CARL P. STILLMAN, R. AGA., U.S.N. (Ret.), IOLA JUHL THELEN,
HELEN R. MILLER, LOUIS J. ROSKY, VIRGINIA COLLETTE, DEBORAH FITZGERALD,
REV. MARK A. CANTREY, WILL RANFELLS, LARRY ANDREWS, JULIA-JEAN STOKES,
and CHARLES A. GOULD, JR., by their attorney, GUYTON P. MALONE,

and respectfully represent to this Court as follows:

1. That the plaintiff, THE NATIONAL ANTI-VIVISECTION SOCIETY, is a not-for-profit corporation organized and existing under the laws of the State of Illinois; that the plaintiff, Rev. MARK A. CAFFEY, is the President and a Director of said corporation; that the plaintiff, GEORGE J. TRAPP, is the Secretary-Treasurer and a Director of said corporation; that the plaintiffs, IOLA JUHL THELEN and HELEN R. MILLER are Directors of said corporation; that the plaintiff, LOUIS J. ROSKY is the Vice President of said corporation; that each of the individual plaintiffs is a member of The National Anti-Vivisection Society and is a citizen and taxpayer of the United States;

2. That the defendant, JAMES SCHLESSINGER, is the duly appointed, qualified and acting Secretary of the Defense of the United States, whose official residence is Washington, D. C. and who is sued herein in that capacity;

3. That the defendant, JOHN L. McLUCAS, is the duly appointed, qualified and acting Secretary of the Air Force of the United States, whose official residence is Washington, D. C. and who is sued herein in that capacity;

4. That the defendant, Gen. IRBY B. JARVIS, is the duly appointed, qualified and acting Commanding Officer of Wright-Patterson Air Force Base, whose official residence is Dayton, Ohio, and who is sued herein in that capacity;

5. That the defendant, Lt. Col. JAMES N. HOLT, is the duly appointed, qualified and acting Officer-in-Charge of the Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, whose official residence is Dayton, Ohio, and who is sued herein in that capacity.

6. That this action arises under the Act of Congress, 78 Stat. 699; USC, Title 28, Section 1346, as hereinafter more fully appears.

7. That venue is proper herein pursuant to 77 Stat. 473; USC, Title 28, Section 1391.

8. That among the stated purposes of the plaintiff, THE NATIONAL ANTI-VIVISECTION SOCIETY, is, through education, "eliminating the practice of using animals in any way, shape or manner for purposes of medical research, medical testing, or medical training"; that each of the individual plaintiffs subscribes to this belief and purpose and is unalterably opposed to the practice of such animal experimentation.

9. That one or more or all of the defendants have caused to be promulgated a purported "Fact Sheet on Research on Beagle Dogs," dated July 17, 1973; said purported "Fact Sheet" is deceptive, erroneous and misleading in referring to "six to nine month old beagles" as dogs, whereas, such animals are puppies, in attempting to convey the impression that the animal experimentation referred to therein was to be conducted under

some form of approval of the Society for the Prevention of Cruelty to Animals, whereas, no such approval had been obtained and has not been obtained, and in referring to the contemplated program as "humane and worthwhile." Said purported "Fact Sheet" is attached hereto as "EXHIBIT A" and made a part hereof.

10. That one or more or all of the defendants have caused to be promulgated a purported "Fact Sheet on Research on Beagle Dogs," dated July 19, 1973, attached hereto as "EXHIBIT A" and made a part hereof; said purported "Fact Sheet" eliminated the reference contained in "EXHIBIT A" to the Society for the Prevention of Cruelty to Animals, while perpetuating the remaining deceptive, misleading and erroneous statements set forth in paragraph 9 of this Complaint.

11. That one or more or all of the defendants have caused to be issued a contract notice announcing the intention of the Air Force to purchase approximately two hundred (200) debarked, purebred, six to nine month old beagles to be used in environmental pollution studies at the Aerospace Medical Research Laboratory, Wright-Patterson AFB, Ohio.

12. Your plaintiffs allege and contend that the defendants, and each of them, and their agents and servants, should be enjoined and restrained from purchasing said beagles, or any substitute laboratory animal, for the purposes set forth in the said "Fact Sheets" and from conducting the "studies" described in said "Fact Sheets" for the following reasons:

(a) the "studies" will not and cannot be conducted in a "humane" fashion since, as a necessary result of such "studies," not less than 50% of the experimental animals will expire as a result of toxic poisoning;

(b) the "studies" are repetitive of previous experiments, the results of which are available to defendants;

(c) the results of the "studies" will be of no value in determining the effect of the various aviation pollutants upon the human system;

(d) the costs involved in conducting such "studies," including the cost of purchasing laboratory animals, the use of government and other public facilities for their conduct, contract payments to be made to those performing the "studies" and similar expenditures, constitute a misuse of public funds;

(e) the performance of such "studies" under the conditions set forth in the "Fact Sheets" and in public statements issued by agents and servants of the defendants has brought, and will continue to bring, this country and its citizens into disrepute in the international community.

WHEREFORE, plaintiffs pray that this Court:

A. Grant an injunction during the pendency of this action and permanently, restraining and enjoining the defendants, and each of their officers, agents, assistants, employees, workers and anyone associated with or acting in concert with them and their successors in office, and each of them, from purchasing beagles, or any substitute laboratory animal, for the purposes set forth in the "Fact Sheets," attached hereto and made a part hereof as "EXHIBITS A and B," or for any other purpose.

B. Grant an injunction during the pendency of this action and permanently, restraining and enjoining the defendants, and each of their officers, agents, assistants, employees, workers and anyone associated with or acting in concert with them and their successors in office, and each of them, from conducting environmental pollution studies described in said "Fact Sheets" upon beagles, or any substitute laboratory animal, or upon any human person without that person's freely given and knowing consent.

C. Grant such other and further relief as to the Court seems proper.



Douglas J. Maloney, Attorney for
Plaintiffs

DOUGLAS P. MALONEY
Attorney for Plaintiffs
100 West Monroe Street - Suite 1911
Chicago, Illinois 60603
CE. 6-1100

FACT SHEET
ON
RESEARCH INVOLVING BEAGLE DOGS

Some months ago, the Air Force issued a contract notice announcing its intention to purchase approximately 200 "de-barked, purebred, six to nine month old" beagles. The dogs are being procured as part of an Air Force contract with the University of California for environmental pollution studies at the Aerospace Medical Research Laboratory, Wright-Patterson AFB, Ohio.

The animals will not be used to test "poison gases" or any chemical or biological warfare agents, as some reports alleged. Rather, the contract specifies that: "Research on offensive chemical or biological warfare agents shall not be performed by contractor professional or technical staff under terms of this agreement." Testing will involve the environmental impact of aviation pollutants. Examples of the tests include establishing safe human exposure limits for: rocket and jet fuels; fire extinguishants used in confined spaces; gaseous products of solvents used in space cabins and other confined areas. The results from these tests will help prevent human illness in the future.

All public laws, as well as principles of laboratory animal care as outlined by the National Academy of Sciences and the Department of Health, Education and Welfare, are strictly followed. The Society for the Prevention of Cruelty to Animals concurs in these principles.

As additional information, "debarking" is a simple, painless, and usually temporary (three to six months) procedure. It is commonly used by university, industrial, and governmental laboratories when large numbers of dogs are to take part in experiments indoors.

It is unfortunate that the adverse national publicity given this humane and worthwhile program was the result of half-truths, unsupported allegations, and innuendoes.

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7300 2107
No.

United States District Court
FOR THE
NORTHERN DISTRICT OF ILLINOIS,
EASTERN DIVISION
THE NATIONAL ARTS DIVISION
SOCIETY, an Illinois not-for-
profit corporation, et al

JAMES SCHLESSINGER, Secretary
of the Defense of the United
States, et al

SUMMONS IN CIVIL ACTION

Returnable not later than . . . days
after service.

DOUGLAS P. MALONEY
100 W. Monroe St. Suite 1911
Chicago, Illinois 60603
CR. 6-1100 Attorney for Plaintiff

FD-111-6-7-22-8000-1105

CIVIL ACTION FILE NO

FOR THE

THE UNITED STATES DISTRICT COURT

Note: Affidavit required only if service is made by a person other than a United States Marshal or his Deputy.

[SEAL]

Subscribed and sworn to before me, a

day of . . . 19 . . .

Deputy United States Marshal.

United States Marshal.

By

MARSHAL'S FEES

Service

Travel

MEMORANDUM OF AGREEMENT ESTABLISHING THE TOXICOLOGICAL CENTER *

This memorandum of 26 June 1956 describes the basis of an agreement among the sponsoring departments and agencies for the support of the Toxicological Information Center of the National Academy of Sciences-National Research Council.

It is agreed that:

1. Establishment and maintenance of a "Toxicological Information Center" is considered essential and meets an urgent need for a central source of toxicological information and advice for operational purposes concerning problems bearing on the health of military and civilian personnel. The Toxicological Information Center will:

a. Provide a full-time service for toxicological information and advice. The Toxicological Information Center will be essentially advisory, and supplement rather than supplant current toxicological activities in the military and other participating agencies. No research projects are to be conducted. The Toxicological Information Center will function as a clearing house and medium of exchange of toxicological data and interpretations thereof.

b. Receive and make available unclassified toxicity data from governmental, industrial, academic laboratories and from other available sources. It will work jointly with the Chemical-Biological Coordination Center of the National Academy of Sciences-National Research Council in the accumulation of unclassified data to develop ultimately a comprehensive file of toxicity information.

c. Foster the exchange of classified toxicological information, maintaining security control so that data developed within any facility of any agency may be available to others under procedures determined by participating agencies.

d. Serve as a stimulus for the declassification, publication and dissemination of toxicological information through appropriate channels.

e. Bring to the attention of the Committee on Toxicology requests: a) for determination of questions of broad policy; b) for recommendation of interim operating Maximal Allowable Concentrations; c) for recommendations of specific toxicological testing or research; d) from the responsible operating

agency to advise on and participate in field studies of toxicity problems.

f. Recommend to the Committee elimination of duplication of expensive toxicological research on a given material when the existence of unnecessary duplication is discerned.

2. There is a continuing year-to-year need for a Toxicological Information Center. A planned mechanism of fiscal support will be undertaken by the departments and agencies represented in proportion to the estimated requirements for this service. The entire budgetary requirements will be reviewed annually and implemented through appropriate channels by designated representatives of the departments and agencies undersigned. Financial support from non-governmental sources will be encouraged. Signatory departments and agencies will be informed of such support in annual reports.

3. Subject to the general policies and procedures of the National Academy of Sciences-National Research Council, the scientific policies and direction of the Toxicological Information Center will be the responsibility of the Division of Chemistry and Chemical Technology with the advice of the Committee on Toxicology and in consultation with the Division of Biology and Agriculture and the Division of Medical Sciences.

4. Each participating agency shall designate a liaison office to serve as a formal channel for all requests for toxicological data and evaluation required by the various departments and bureaus of said agency.

5. Within each participating department or agency, mechanisms will be provided to bring toxicological data available within that agency to the attention of the Toxicological Information Center. These mechanisms must be subject to security requirements.

6. Each contributing agency shall be permitted to have liaison representation on the Committee on Toxicology.

7. It is agreed that the Toxicological Information Center will be physically located in the Washington area.

* The name was changed from the Toxicological Information Center to the Advisory Center on Toxicology in September 1959.

Listing of Additional Materials Considered by the ad hoc Sub-committee Reviewing the Toxicology Research Program of the 6570th Aerospace Medical Research Laboratories. Copies of all items are submitted herewith for Air Force Records

1. Outline of rationale for using dogs (Oral briefing by Dr. Thomas on 29 September 1973).
2. The dog, as an experimental animal.
3. Clinical laboratory values of beagle dogs. Robinson, F. R. and Ziegler, R. F. Laboratory Animal Care 18:39-49 (1968).
4. The beagle as an experimental dog. (excerpts). A. C. Anderson and L. D. Good eds. Iowa State University Press, Ames, Iowa.
5. Panel on carcinogenesis report on cancer testing in the safety evaluation of food additives and pesticides. Food and Drug Administrative Advisory Committee on Protocols for Safety Evaluation. Toxicol. Appl. Pharmacol. 20:419-438 (1971).
6. Suggested principles and procedures for developing experimental animal data for threshold limit values for air. Stokinger, P. E. American Conference of Governmental Industrial Hygienists. (Tentative Documentation).
7. Methods in Toxicology. G. E. Paget, ed. F. A. Davis Co., Philadelphia (1970).
8. PL 91-596. The Occupational Safety and Health Act of 1970.
9. Aerospace toxicology. I. Propellant Toxicology. Back, K. C. Federation Proc. 29:2000-2005 (1970).
10. Aerospace toxicology. II. Toxicological evaluation of materials associated with spacecraft. Back, K. D. Federation Proc. 29:2006-2009 (1970).
11. The AMRL Mission, Wright-Patterson AFB, Ohio. Air Force/56780/ 11 June 1973-1000.
12. Resumes of THRU (Univ. of Calif.) Personnel.
13. The determination of the inotropic effect of exposure of dogs to bromotrifluoromethane and bromochlorodifluoromethane. Van Stee, E. W., Diamond, S. S., Harris, A. M., Horton, M. C., and Back, K. D. Toxicol. Appl. Pharmacol. 27: in press (1974).

14. Viewgraphs accompanying verbal presentation outlining AMRL toxicology research program.
15. Viewgraph accompanying verbal presentation of toxicity tests on Air Force presentation.
16. Viewgraphs accompanying verbal presentation of pathology branch, toxic hazards division.
17. Viewgraphs accompanying verbal presentation of animal utilization.
18. Correspondence relating registration and inspection of AMRL animal facilities.
19. List of equipment in Toxic Hazards Division.
20. News article "Pups Study Has No Bite", C. Stough, Dayton Daily News, 17 September 1973.
21. Organization chart of AMRL Toxic Hazards Division.
22. 1973 progress reviews of toxicology projects.
23. Research and development planning summaries.
24. Engineering service project plans.
25. Research and development management reports.
26. Program of Fourth Conference on Environmental Toxicology, October 1973.
27. AFSC technical facility reports.
28. Inhalation toxicology of low-molecular-weight fluorocarbons.
29. Experimental protocols for bioenergetics and red blood cell metabolism.
30. The mechanism of the peripheral vascular resistance change during exposure of dogs to bromotrifluoromethane. Van Stee, E. W. and Back, K. C. Toxicol. Appl. Pharmacol. 23:428-442 (1972).
31. Research protocols for projects by THRU.

32. Acute inhalation toxicity of monomethylhydrazine vapor. Haun, C. L., MacEwen, J. D., Vernot, E. H. and Eagan, G. F. Am. Ind. Hyg. Assoc. J. 31:667-677 (1970).
33. Resumes of AMRL Toxic Hazards and Veterinary Medicine Divisions' personnel.
34. Correspondence relating to dog devocalization.
35. Background report on Aerospace Medical Division of Air Force Systems Command including:
 - a. Mission statement
 - b. Civil action suit 73C-2181 in U.S. District Court for the Northern District of Illinois Eastern Division.
 - c. History of coordination of toxicology R and D with NAS/NRC.
 - d. 1972 Medical and biological sciences technology coordinating paper (excerpts).
 - e. Narratives of current toxicology projects.
 - f. Publications list of Toxic Hazards Division.
36. American Humane Association report of inspection of 6570 AMRL.
37. Report of visit by Dr. LeBürge to WPAFB.
38. The operant control of vocalization in the dog. Salzinger, K. and Waller, M. B. J. Exptl. Anal. Behavior 5:383-389 (1962).
39. Dogs. Standards and guidelines for the breeding, care, and management of laboratory animals. Institute of Laboratory Animal Resources, National Research Council, National Academy of Sciences. 1973.
40. Guide for the care and use of laboratory animals. Institute of Laboratory Animal Resources, National Research Council, National Academy of Sciences 1972.
41. 40CFR180.36 EPA Pesticide Chemical Safety Proposed Toxicology Guidelines.
42. Procurement specification (contract clause) V. Kennel-produced dogs. NIH-USDHEW. Institute of Laboratory Animal Resources, National Research Council, National Academy of Sciences 1969.

43. Attachment VIII. Annual report of research facilities. USDA Animal and Plant Health Service 1972.
44. 9 CFR 1 Animals and Animal Products, Animal and Plant Health Inspection Service 1 January 1973 (exerpts).
45. Debarking in a kennel: Technjc and results. Anderson, A. C. Vet. Med. 50: 409-411 (1955).
46. Viewgraphs accompanying verbal presentation on Aerospace Medical Division.
47. Viewgraphs accompanying verbal presentation on Aerospace Medical Research Laboratory.
48. 1972 Annual report on laboratory animal welfare act of 1966 as amended by animal welfare act of 1970. U. S. D. A. Animal and Plant Health Inspection Service.
49. Viewgraphs accompanying verbal presentation on organization and function of AMRL.

**SITE VISIT OF AD HOC PANEL (NAS/NRC) TO WRIGHT - PATTERSON
AFB FOR REVIEW OF AIR FORCE TOXICOLOGY PROGRAM**

**Location: Toxic Hazards Division (AMRL)
Bldg. 79, Area B, Wright-Patterson AFB, OH**

AGENDA

3 October 1973

1300 - 1700 Tour of Vivarium by Dr. Melby

193 - 2300 Executive Session

4 October 1973

**0830 - 0845 Welcome and Introductory Remarks
(Col F. Doppelt, Commander, AMRL)**

**0845 - 0915 Aerospace Medical Division Overview
(Col N. Clarke, Director of R and D, AMD)**

**0915 - 0945 Air Force Requirement for Toxicology R and D
(Maj D. Beatty, AMD/RDB)**

**0945 - 1015 Toxic Hazards Division Program
(A. Thomas, M. D., Director)**

1015 - 1030 Coffee Break

**1030 - 1100 Veterinary Care Program
(Lt Col G. Anstadt and Maj E. McConnell)**

**1100 - 1145 Tour of Vivarium Facilities
(Bus Transportation Provided)**

**1145 - 1245 Lunch, Executive Dining Room, Building 16
(Bus Transportation Provided to and From Lunch)**

1255 Reconvene in Building 79

**1300 - 1330 Toxicology, Pharmacology and Metabolism of
Halogenated Fire Extinguishing Agents
(Maj E. Van Stee)**

1330 - 1345	Discussion
1345 - 1400	Ultrastructural Effects of Toxic Exposure (Maj. N. McNutt)
1400 - 1415	Discussion
1415 - 1445	Current Exposure Studies in the Toxic Hazards Research Unit (University of California) (Dr. J. D. MacEwen, Director)
1445 - 1500	Discussion
1500 - 1515	Analytical Chemical Aspects of Exposure Studies (University of California) (E. Vernot, Assistant Director)
1515 - 1530	Discussion
1530 - 1545	Coffee Break
1545 - 1700	Tour of Toxic Hazards Division Facilities and Dis- cussion with Senior Investigators in Their Laboratories
1700	Return to Imperial House, North for Panel Working Session
<u>5 October 1973</u>	Building 79
0830 - 1200	Panel Executive Session (All AF and U. C. Scientists will be available on demand for further discussion, if required)
1200 - 1300	Box Lunch for Panel Members
1300 - 1500	Panel Working Session (Secretarial Help Available)

6570 AMRL REGULATION
NO. 163-1

6570TH AEROSPACE MEDICAL RESEARCH LABORATORY
Wright-Patterson Air Force Base, Ohio
31 January 1969

Veterinary Service

USE OF ANIMALS

PURPOSE: To establish the policy and assign responsibilities for the management, care and use of all experimental animals, animal supplies, and animal facilities of the 6570th Aerospace Medical Research Laboratory.

1. Policy. The Chief, Veterinary Medicine Division (MRV), shall be charged with the responsibility for the supervision, management and operation of the experimental animal program. Divisions engaged in biological research will requisition the minimum number of animals needed for projects and will be responsible for the judicious use of those animals in compliance with this regulation and all other directives concerning the use of animals as experimental subjects. The policies stated herein are directed toward insuring sound laboratory animal medicine. They are not to be all encompassing and are not to be interpreted to limit additional efforts toward providing for the health, welfare, care and management of the animals used in Aerospace Research.

2. References:

- a. AFR 169-2, "Laboratory Animals in DoD Research."
- b. Public Law 89-544, "Laboratory Animal Welfare Act," 24 August 1966.
- c. "Laboratory Animal Welfare," Agricultural Research Service, Department of Agriculture, Federal Register Vol. 32, No. 37, 24 February 1967.
- d. "Guide for Laboratory Animal Facilities and Care" prepared by the Committee on Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.
- e. AFM 163-5, "Care and Management of Laboratory Animals."
- f. AFR 169-94, "Publication of Medical and Related Technical Papers."

This regulation supersedes 6570 AMRLR 163-1, 15 Sep 65. (See summary of revisions deleted, or added material on last page below signature element.)

OPR: MEV

DISTRIBUTION: 6570 AB Gp (CPAP), S

3. Responsibilities:

a. The Chief, Veterinary Medicine Division, 6570 AMRL, will be responsible for:

(1) Animal Care Section:

(a) Receiving, quarantine, processing, housing, feeding, watering, immunizing, and standardizing all animals owned or in the custody of the 6570 AMRL, including resident contractors.

(b) Advising, instructing, and monitoring personnel of all sections in the proper handling, transporting, restraining, etc., of experimental animals.

(c) Issuing animals for experiments and disposing of dead animals after necropsy examinations have been made.

(d) Monitoring requests for animals and budgeting for special food, cages, equipment and other supplies required in the program.

(e) Inspecting sources of supply for laboratory animals.

(f) Rendering post-operative and longevity treatment to animals as prescribed by the researcher upon completion of a test.

(g) Maintaining records on animals to indicate date of purchase, vendor, species of animals, medication, medical history, and other pertinent data.

(h) Operating the incinerators or other means of disposal of animal carcasses, waste materials, etc.

(2) Research Support:

(a) Performing or assisting with surgical procedures as may be required by the project officers in conducting their projects.

(b) Rendering nursing and post-operative care to all animals that have been subjected to surgical procedures.

(c) Maintaining a surgical supply system that will assure adequate instruments, surgical accessories and surgical logistics for the operating room.

(d) Providing a necropsy room for investigators' use. Gross and histopathologic support will be coordinated with the Pathology Branch, Toxic Hazards Division.

(e) Providing an animal radiology service.

(f) Providing a laboratory animal medicine consultation service for inquiring investigators.

(g) Monitoring all biomedical research programs to ensure that animal research subjects are treated in accordance with the standards for humane handling, care, treatment, and transportation established by the Secretary of Agriculture in "Laboratory Animal Welfare" and in the "Guide for Laboratory Animal Facilities and Care" prepared by the National Academy of Sciences - National Research Council.

b. Chiefs of the divisions and branches of the 6570 AMRL are responsible for:

(1) Humane and proper treatment of animals during experiments conducted within their jurisdiction.

(2) Coordinating all animal requirements with the Chief, Veterinary Medicine Division, to insure that space, cages, food, special equipment, etc., will be available when animals are received.

(3) Immediately notifying MIV when animals are excess to requirements of the program.

c. Each investigator is responsible for:

(1) Administering anesthetic or analgesic agents to animals that are being used for experiments when painful procedures are necessary.

(2) Providing recovery surveillance of animals under anesthetic agents to prevent injuries and post anesthesia sequelae.

(3) Using only that restraint necessary to safely control but never so severe as to abuse the animal.

(4) Minimizing the use of animals by exhausting all other research methods available.

(5) Practicing prompt euthanasia of animals after completion of acute experiments.

(6) Informing MIV of any animal problems or aftercare needed for their animals.

(7) Each manuscript pertaining to research involving animal experimentation must be accompanied by the following statement: The experiments reported herein were conducted according to the "Guide for Laboratory Animal Facilities and Care," 1965, prepared by the Committee on the Guide for Laboratory

Animal Resources, National Academy of Sciences - National Research Council; the regulations and standards prepared by the Department of Agriculture; and Public Law 89-544, "Laboratory Animal Welfare Act," 24 August 1966.

d. Each contract monitor will be responsible for insuring that the contractor maintains research animals in accordance with the documents listed in paragraphs 2b, 2c, and 2d. Each contract or grant involving laboratory animals will contain a clause citing the referenced directives.

4. Procedures:

a. Access to Veterinary Medicine Facility. To prevent spread of infectious diseases, access to the animal rooms will be with the approval of the Chief, Veterinary Medicine Division.

b. Veterinary Consultation Services. Consultation services relating to selection of species, strains, dietary problems, housing, and other facets of animal use and care will be available to all project officers from the Veterinary staff.

c. Special drugs and equipment will be furnished by the investigator.

5. Records:

a. Office of Record. MRV will maintain the record copy of the health records of research animals created by this regulation.

b. Disposition of Records. Records maintained by MRV will be permanent as a part of the Veterinary Clinical Records. (Authority: Para 151105.b, AFM 181-5.) All other records will be destroyed when they have served the purpose for which created. (Authority: Para 050201, AFM 181-5.)

OFFICIAL

C. H. KRATOCHVIL, Colonel, USAF, MC
Commander


STANLEY L. BLECHA, Colonel, USAF
Chief, Support Services Division

Summary of Revised, Deleted, or Added Material

Quotes current applicable references (Para 2). Extensively deletes information which no longer applies. Delineates responsibilities of the Chief, Veterinary Medicine Division, to ensure that animal research subjects are treated in accordance with new standards established for laboratory animal welfare and care (Para 3). Establishes revised guidelines for division chiefs, investigators and contract monitors as applies to animal use (Para 3b, c, d). Deletes pathology service for the Division and outdated policy for requesting laboratory animals.

12 July 1973

Veterinary Service

UTILIZATION OF ANIMALS IN RESEARCH

This regulation establishes policy, assigns responsibility and outlines procedures concerning the use of experimental animals, supporting items and facilities. Included are minimal acceptable standards for the health and welfare of experimental animals, control of zoonotic diseases, management of facilities and releasing of public information pertaining to the care and use of laboratory animals within the research program of the 6570th Aerospace Medical Research Laboratory.

1. References:

- a. AFR 160-124, "Radioisotope Licenses and Permits," and WPAFB Sup 1 thereto.
- b. AFR 161-6, "Control of Communicable Diseases in Man."
- c. AFM 163-5, "Care and Management of Laboratory Animals."
- d. AFR 169-2, "Laboratory Animals in DoD Research," and AMD Sup 1 thereto.
- e. WPAFBR 161-1, "Safe Use of Radioactive Materials."
- f. WPAFBR 163-1, "Rabies Control."
- g. 6570 AMRLR 190-2, "ANRL Clearance Procedures for Release of Information to the Public."
- h. Public Law 89-544, "Laboratory Animal Welfare Act," 1966 and ensuing amendments.
- i. Public Law 91-579, "The Animal Welfare Act," 1970.
- j. "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.
- k. Code of Federal Regulations, Title 42, Chapter 1, Subchapter F.
- l. Veterinary Medicine Division Letter, 1 Nov 72, "Standards and Operational Procedures for Investigator Personnel Using Vivarium Facilities."

2. Policy. Animals intended for use in research shall be provided care and treatment in accordance with the highest standards of humane procedures.

This regulation supersedes 6570 AMRLR 163-1, 31 Jan 69. (For summary of revised, deleted or added material, see signature page.)

OPR: AMRL/VM

DISTRIBUTION: AMD/DAP;F;X (USAF/Med Cen/VT)

These standards are extended to all species of research animals, as set forth in the references listed above. All matters relating to the procurement, care, and management of experimental animals will be fully supported.

3. Responsibilities:

a. Veterinary Medicine Division will:

- (1) Be responsible for the supervision, management and operation of the experimental animal program.
- (2) Coordinate annual animal requirements among the research Divisions.
- (3) Review proposed project protocols and provide consultation to investigators on the selection and use of experimental animal models.
- (4) Initiate animal procurement based on approved protocols, receive, quarantine, standardize and provide or supervise professional medical care for all animals used in the research programs of this Laboratory.
- (5) Approve laboratory animal sources of supply and perform preacceptance examinations on experimental animals as indicated.
- (6) Provide necessary support such as veterinary medical care, professional and/or technical assistance, facilities, and animal euthanasia for approved projects.
- (7) Advise, instruct and monitor procedures used by AMRL personnel regarding the proper handling, humane treatment, transport, restraint and euthanasia of experimental animals.
- (8) Deliver laboratory animals to appropriate locations within the Laboratory for use by investigators.
- (9) Monitor decentralized colonies and individual experiments regarding proper care and treatment of research animals.
- (10) Initiate procurement of feeds, bedding materials, ancillary equipment, surgical and support supplies as required for routine animal use.
- (11) Direct disposal of carcasses and maintain a cold room for the deposit of such carcasses submitted for necropsy, tissue collection, or disposal.
- (12) Maintain an animal radiology service for use with the research animals of the Laboratory.

(13) Review at least semi-annually the status of the employee health examination program applicable to each research Division whose personnel handle experimental animals, and report findings to AMRL/CC.

b. Research Divisions Using Animals Are Responsible for:

(1) Ensuring that project protocols, signed by the branch chief, are coordinated with the Veterinary Medicine Division. Protocols shall include

(a) Title, project/task/work unit number, investigators, purpose and brief description of experimental design and methodology.

(b) Species, age, sex and number of animals required.

(c) Schedule of animal use, and anticipated project initiation and completion dates.

(d) Type of other support required, such as professional and/or technical assistance, facilities and equipment.

(2) The humane and proper treatment of animals during experiments conducted within their jurisdiction.

(3) Ensuring that anthrozooses control measures are followed to include:

(a) Each Division Office shall establish a single file folder listing those personnel whose duties require them to work with experimental animals. The file should contain:

(1) Name

(2) Date of last physical examination

(3) Date last Tine Test

(4) Date last Chest X-Ray and Special Immunizations

applicable to each individual.

(b) All personnel, including contract personnel, working with experimental animals receive physical examinations annually as scheduled through the USAF Medical Center, Building 40, Area B. Those personnel working with simian primates must receive an annual chest radiograph and biannual tuberculin test, and/or other examinations as may be directed by the Director, Base Medical Services.

(c) Personnel wear protective face masks when working with primates or in areas where infectious disease is a risk. Street clothing is to be replaced or covered with protective clothing prior to entering animal rooms and when working with laboratory animals. Following use, contaminated clothing should not be worn in other areas.

(d) Only authorized personnel shall enter animal holding rooms or rooms housing animals during ongoing experimentation.

(e) Only qualified individuals shall catch and restrain laboratory animals regardless of species.

(4) Notifying AMRL/VM of anticipated annual animal requirements with sufficient lead time to accomplish routine procurement.

c. Investigators will:

(1) Coordinate with the Research Support Section, AMRL/VM, regarding animal model of choice, surgical support, restraint assistance, anesthesia, or other support procedures that are anticipated for research design.

(2) Coordinate with the Research Support Section, AMRL/VM, regarding procedures for animal procurement, assignments, issue, investigational usage and disposition.

(3) Provide a copy of their approved experimental protocol to the Veterinary Medicine Division prior to project initiation.

(4) Practice humane care and prompt euthanasia of animals upon completion of experimentation.

(5) Ensure that animal carcasses and tissues for disposal are placed in the cold room at the Veterinary Medicine Division. Such carcasses must be properly marked and identified including date of death, investigator, animal number, and disposition desired. Carcasses will not be held for necropsy or tissue collection longer than two normal work days. All tissues and carcasses must be sealed in plastic bags and/or boxes to prevent escape of body fluids.

(6) Ensure that any live animal, carcass, tissue, or waste which contains radioactive material is properly identified and handled according to appropriate policies and regulations (see References).

(7) Inform the Research Support Section, AMRL/VM, of post experimental animal care requirements and/or final disposition instructions.

(8) Ensure that all manuscripts, papers and reports, involving animal experimentation are accompanied by the following statement:

"The experiments reported herein were conducted according to the "Guide for Laboratory Animal Facilities and Care," prepared by the Institute of Laboratory Animal Resources, National Research Council."

d. Contract Monitors will:

(1) Coordinate all proposed contracts involving the use of research animals with Chief, Veterinary Medicine Division, prior to contract approval. All such contracts require compliance with paragraph lh and lj.

(2) Determine contractor compliance with the provisions of AFR 169-2 and AMR Supplement 1 thereto. The Veterinary Medicine Division provides professional consultation, technical and/or on-site inspection as required.

4. Importation and/or Interstate Shipment of Agents and/or Specimens:

a. Various Federal agencies have regulations covering the importation, interstate shipment, and safe packaging of etiologic agents and diagnostic specimens. Compliance must be with the Code of Federal Regulations, Title 42, Chapter 1, Subchapter F.

b. The Biohazards Control Officer of the Center for Disease Control, Atlanta, Georgia, shall be contacted for guidance prior to the importation, or interstate shipment subsequent to importation of etiologic agents pathogenic to man or animals.

5. Treatment of Wounds. Individuals bitten by laboratory animals will report immediately to the Dispensary, Building 40, Area B, for treatment. It is imperative that an immediate identification of the animal be made, such as tattoo, cage number or location, so that quarantine can be effected. The Veterinary Medicine Division, Building 858, Area B, is the quarantine authority for all research animals which inflict injury to biomedical research personnel.

(1) When a bite incident occurs, the supervisor will report the incident to the Chief, Veterinary Medicine Division.

(2) Skin penetrating injuries caused by equipment which comes into direct contact with laboratory animals should be immediately reported to the appropriate medical authority for treatment.

6. Visitors and Tours. Only authorized persons accompanied by an appropriate AMRL representative shall be permitted to visit or tour the animal research facilities.

7. Stray Animals. The Veterinary Medicine Division shall not, under any circumstances, accept stray animals, pets or donations of animals from any source.

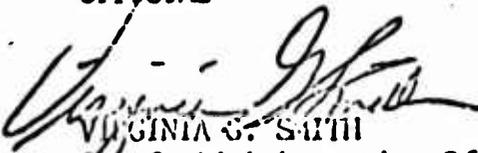
8. Documentation:

a. Office of Record. AMRL/VM is designated the Office of Record and will maintain the record copy of the health records of research animals.

b. Disposition of Records. Research animal records will be retired as permanent records. (Auth: Table 163-1, Rule 14, AFM 12-50).

OFFICIAL

FREDRIC F. DOPPELT, Colonel, USAF, MC
Vice Commander


VIRGINIA S. SMITH
Chief, Administration Office

[SUMMARY OF REVISED, DELETED OR ADDED MATERIAL]

Generally updates references and regulation. Deletes old paragraphs 3a(1) and 3a(2) and incorporates responsibilities at Division level. Outlines requirement for coordination of animal use protocols with AMRL/VM. Provides for an anthrozooses program in Divisions using animals. Establishes revised guidelines for Division Chiefs, Investigators and Contract Monitors as applied to animal use. Adds information on importation, interstate shipment of agents and specimens.

QUALITY CONTROL PROGRAM

'General Statements

1. Procure animals only from approved sources. ("Animals for Research" published by NAS)
 - a. Dealer must be registered (see Fed. Reg. - 1973)
 - b. Use of past experience.
 - c. Liaison with other government agencies as to current disease status and trends at other facilities.
 - d. Procurement must comply with Air Force requirements, which are often more stringent than required by other buyers.
 - e. Invite prospective suppliers to submit samples of animals for examination (particularly rodents).
2. Verification of Quality after animal arrives (at point of arrival and during transportation).
 - a. Parasite exam
 - b. T.B. testing of primates
 - c. Personal observations - physical exam (daily health check)
 - d. Bacteriology
 - e. Serology
 - f. Gross, Histo and Clinical Pathology
 - g. Check weight for age
 - h. Treatment of spontaneous disease if indicated.
3. Procurement of standardized feeds.
4. Quarantine periods (vary in time) on all animals.
5. Personnel keep current with state of the art by attending short courses, symposiums, and scientific meetings.

DOGS

1. Physical exam on arrival followed by daily clinical observation during quarantine and while on test.
2. Treatment of sick animals as indicated prior to or during test.
3. Vaccination - performed prior to arrival at AMRL. Includes distemper, infectious hepatitis, leptospirosis and rabies.
4. Parasites - fecal and microfilaria exams on arrival. Additional exams if indicated. Routine dipping for external parasites unless contra-indicated by experimental protocol.
5. Animals weighed and followed during quarantine period.
6. Brucellosis - titers (if any) determined on all new arrivals. Positives and suspects are confirmed by culture and are eliminated from the colony and autopsied.
7. Clinical Pathology - PCV determined at release from quarantine status. Clinical pathology exam (see THP handout for details) on all animals for use in THRU at least twice at two-week intervals, prior to test. Same procedure while on test.
8. Necropsy of all animals which die spontaneously prior to and while on test.

MONKEYS

1. Close clinical observation maintained during quarantine and while on test (7 days per week); therapy initiated as required.
Primates routinely held 30 days by vendor and 60 days at AMRL/VM prior to release.
2. Tuberculin Testing (Intrapalpebral - mammalian tuberculin) - For release from quarantine all animals must have had 5 successive negative tests at two week intervals. If reactor is found in group, then remainder of primates in group must have five negative tests at two week intervals. No primates are released for test during this time.
3. Parasites - intestinal parasites are monitored by fecal exams during quarantine period. Infested animals treated as indicated.
4. Stool cultures performed if indicated.
5. Weight Determination - weighed at beginning and end of quarantine period and while on test bi-weekly.
6. Clinical Pathology - PCV determined prior to release from quarantine. Clinical Pathology analyses are performed at least two times (minimum of two week interval) prior to and while on test.
7. Any monkey that dies during quarantine or while on test is necropsied.

RABBITS

1. Random sample (5 - 10 animals per group) for necropsy to evaluate endemic disease parameters.
2. Daily clinical observations prior to and while on test.
3. Routinely treat all animals for ear mites.
4. Composite fecal exam for intestinal parasites within two weeks of arrival. Skin scrapings for external parasites.
5. Nasal swabs taken for culture if indicated.
6. Weigh all animals prior to and while on test.
7. Hematology and selected clinical chemistries if indicated by experimental protocol.

GUINEA PIGS

1. Random sample of all new lots (5 - 10 animals per lot) for necropsy exam.
2. Daily clinical observations (prior to and while on test).
3. Necropsy of animals that die prior to or while on test.
4. Monitoring for internal and external parasites (skin scrapings, anal tapes, fecal exam) during quarantine. Same as for mice and rats.
5. Growth curve while in logarithmic phase of growth prior to and during experiment.
6. Selected clinical pathology as indicated by experimental protocol.

HAMSTERS

1. Random sampling of new shipments (10 animals per lot) for gross, histopath and bacti (where indicated). Followed by a second random sample of 10 in seven days. Necropsy is directed toward pulmonary disease.
2. Daily clinical observations prior to and while on test.
3. Necropsy of animals dying prior to or while on test.
4. Monitored for internal and external parasites during quarantine period (same as for mice/rats).
5. Growth curve while in logarithmic phase of growth prior to and during experiment.
6. Pooled blood samples for clinical pathology as indicated by experimental protocol.

RATS & MICE

1. Random sampling for necropsy during quarantine period (10 animals per lot). Directed primarily toward Chronic Respiratory Disease. Includes bacteriology (Mycoplasma culture). Followed by a second sample of 10 animals in seven days.
2. Daily clinical observations prior to and while on test.
3. Composite fecal exams and anal tapes for intestinal parasites.
4. Skin scrapings for external parasites.
5. Necropsy of spontaneous deaths prior to and while on test.
6. Growth curve while in logarithmic phase of growth prior to and during experiment.
7. Clinical pathology on blood sera (individual rats and pooled mice) as indicated by experimental protocol.