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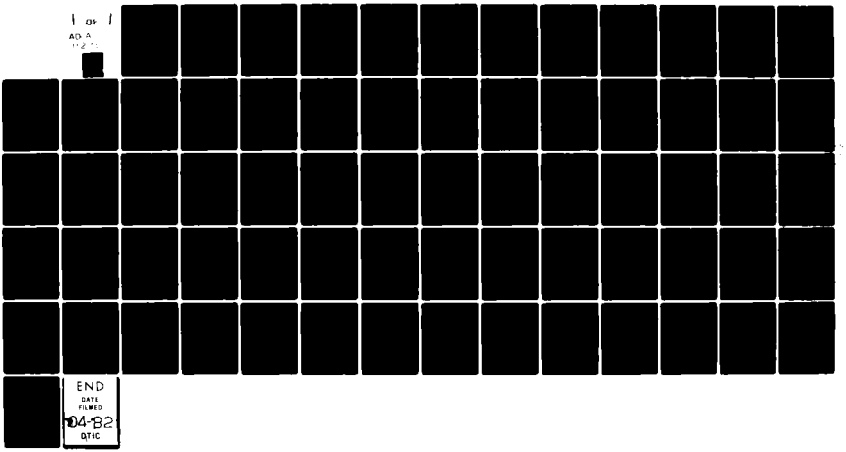

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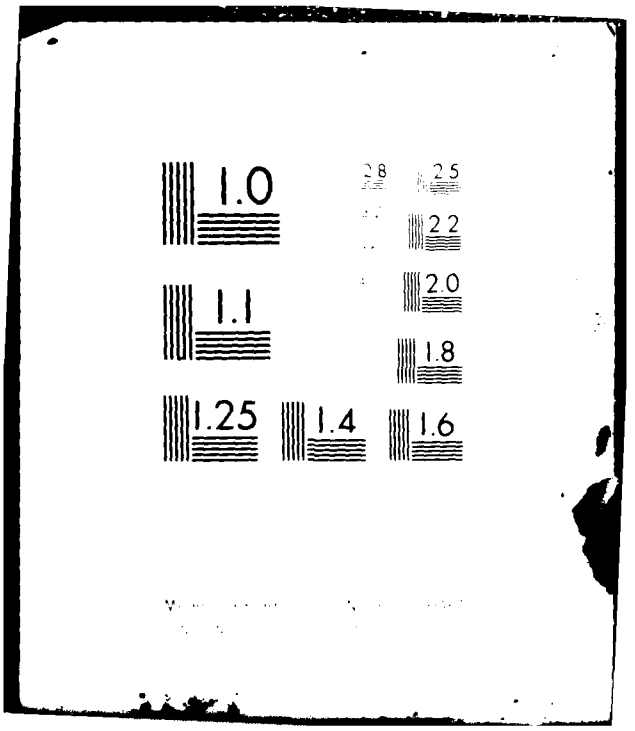
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MAMMALIAN TOXICOLOGY TESTING: PROBLEM DEFINITION STUDY

TECHNICAL PLAN (U)

by
R. A. Wynveen and R. H. Reuter

March, 1981

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

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Cleveland, OH 44122

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Plans for the technical aspects of an Applied Mammalian Toxicology Research/Testing Facility are summarized in this report. Reasons why toxicology testing is needed are reviewed. The plan cites the types of tests needed, those that should be carried out at a new or renovated facility and those extramurally are reviewed. The approach was taken from a scientific point of view. The requirements result from both regulatory and nonregulatory viewpoints. Certain portions, such as basic toxicology research and personnel testing, were not included.

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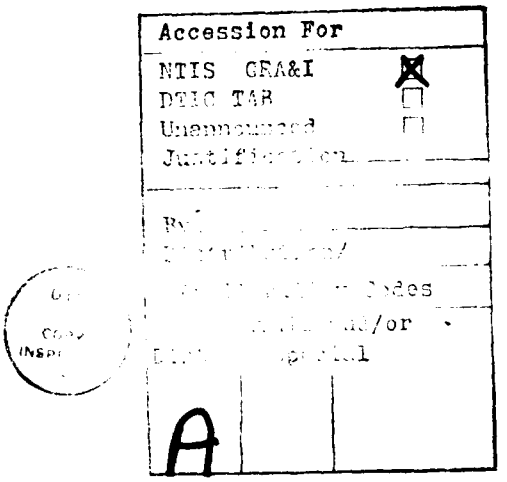
Report Subtitle	Life Systems, Inc. Report Number
Final Reports--	
Part 1. Comparative Analysis Report	LSI-TR-477-2
Part 2. Facility Installation Report	LSI-TR-477-3
Part 3. Impact of Future Changes Report	LSI-TR-477-4



FOREWORD

Reports for this Contract, DAMD17-81-C-1013, consist of three major final reports and twelve supporting documents. The Contract title, MAMMALIAN TOXICOLOGY TESTING: PROBLEM DEFINITION STUDY, is the main title for all the reports. Individual reports are subtitled and referenced with Life Systems, Inc. report numbers as detailed below. Please note that the Life Systems report numbers in test references are shortened. In the Defense Technical Information Center (DTIC) data base the reports are identified by the complete report numbers (i.e., LSI-TR-477-XXX) and complete numbers must be used for retrieval.

Report Subtitle	Life Systems, Inc. Report Number
Final Reports--	
Part 1. Comparative Analysis Report	LSI-TR-477-2
Part 2. Facility Installation Report	LSI-TR-477-3
Part 3. Impact of Future Changes Report	LSI-TR-477-4
Supporting Documents--	
Technology Changes Impact on Testing Requirements	LSI-TR-477-14
Quality Assurance Plan	LSI-TR-477-17A
Capability Modules	LSI-TR-477-19B
Technical Plan	LSI-TR-477-20A
Equipment Plan	LSI-TR-477-21A
Personnel Plan	LSI-TR-477-23A
Inhalation Chambers and Supporting Equipment Survey	LSI-TR-477-26A
Equipment List for Modules	LSI-TR-477-28B
AMTR Protocol/Pricing Report	LSI-TR-477-29A
Global Army Toxicology Requirements	LSI-TR-477-31A
Comparison Toxicology Test Costs	LSI-TR-477-36A
Annual Testing Capacity	LSI-TR-477-38A

SUMMARY

The study under which this report was prepared addressed the Army's global toxicology requirement, evaluating alternatives for meeting a portion of these requirements and establishing conceptualized plans for adding new capability to carry out a portion of the requirement. Of particular importance, is that the Technical Plan prepared is applicable whether the Facility is operated by the Government or a contractor.

Many reasons exist why toxicology testing is needed by the Army. Some tests are mandated by law. Others must be done because they are part of good business practices or for ethical and moral reasons.

The Technical Plan reviews the types of tests that are needed, those that should be carried out in a new or renovated facility and those that could be done extramurally.

In contrast to the Management Plan, this plan viewed the new or added toxicology testing capabilities from the science point-of-view. It was prepared after the Army's toxicology requirements were identified.

Of the many assumptions cited, it should be noted that all science be done in the facility must be of good quality for research and testing purposes. Of particular importance was that all regulations relating to conformance to Good Laboratory Practice be met.

Although the plan covered mammalian toxicology research/testing it did not cover such things as basic toxicology research, occupational health aspects or health hazard assessment.

The Facility was organized to include six major business functions including administration, financial, quality assurance, etc. An organizational chart was provided, depicted as a government-owned, contractor-operated Facility. The results nevertheless would be equally true if it was a Government-owned, Government-operated Facility or a contractor-owned, Government-operated Facility. It is important to note that the study did not provide for selecting the total capability to be incorporated but limited to toxicology testing and, through a subsequent redefinition, to include applied mammalian toxicology research.

Although the actual capability incorporated must be decided by the Medical Research Development Commander/Staff, recommendations were made regarding the minimum a Facility should provide. The latter included, for example, a minimum of four routes of exposure (oral, inhalation, dermal and ocular).

Seven Army business environments were identified which require toxicology technology. Major ones were identified during a typical life cycle from the research, development, test and engineering phase to ultimate demilitarization of Army developed or purchased materiel.

A total of 19 specific types of Army mammalian toxicology tests were identified. Type one, for example, was the acute rodent oral test on one species with the outcome viewed for general toxicology results. Four major genetic toxicology

tests were identified including standards for detecting gene mutations. It was envisioned that the selected capability should be implemented in two stages. Further, each stage should be built-up incrementally. The two stages were identified as the initial capability and the growth capability.

It was noted no major toxicology research/testing capability exists able to handle all the routes of exposure that reflect the Army's requirements. Of particular importance to the Army are the unique exposures that must be reflected in the routes of exposure selected. These include troop exposures associated with weapons systems as well as environmental exposures the general public experiences when living near Army activities.

The tier testing methodology was strongly recommended and guidelines were presented.

Two sites were selected for adding to the Army's Applied Mammalian Toxicology Research/Testing Capability: the Letterman Army Institute of Research and the Hunters Point. The floor plans for each of the Facilities were reviewed. The former, for example, has approximately 325,000 square feet of space as being the maximum available.

The planning effort concluded, the addition of new capability and capacity is recommended. The modular design permits the decision-makers the option to readily pick and choose which capabilities and capacities are desired based upon requirements, priorities, budgets, personnel resources, etc. The Facility must provide for scientifically sound technical results, able to be scrutinized by peer groups, regulatory agents and standard and criteria developers.

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INTRODUCTION

The present document summarizes that portion of the Mammalian Toxicology Testing: Problem Definition Study related to the Technical Plan for the added toxicology research/testing capability.

Background

The Problem Definition Study addressed the Army's global toxicology requirements, evaluated alternatives for meeting a portion of these requirements and conceptualized plans for adding new capability to carry out a portion of the requirements. The portion carried out in a new, added Facility could be operated by the Government or a contractor. This Technical Plan (Plan) is equally applicable to either mode of operation.

Why Mammalian Toxicology Testing Needed

There are many reasons why toxicology testing is needed. Some tests are mandated by law. Others must be done because they are part of good business practices or for ethical and moral reasons.

Each user of the new or added capability (call the Facility) will have one or more reasons for doing so. Besides complying or demonstrating conformance to laws and regulations, they can include generating data to obtain permits and licenses, obtaining approval to manufacture or continue to manufacture chemicals, as part of carrying out effective drug and vaccine development processes, to develop testing methodologies for Army-unique environments and materiel, to establish standards and criteria for occupational health in laboratories, in production plants, in field training and for combat, etc.

Regulatory Requirements

There is an extensive list of public laws that require toxicology testing and affect a toxicology research facility's design and operation. Appendix 1 contains a summary of the 15 major public laws relating to toxicology. These laws affect the Army activities associated with hazardous and toxic substances, pesticides development, munitions manufacturing, foods, drugs and cosmetics, etc.

Non-Regulatory Requirements

Although regulatory requirements are the most visible, non-regulatory requirements for toxicology testing may be extensive. These are the types of tests needed by The Surgeon General to establish, for example, standards and criteria for Army personnel not covered by the Occupational Safety and Health Act. In addition, the non-regulatory requirements can have as their objectives:

1. To prevent decrements in soldier performance,
2. To reduce the need for or level of disability compensation payments,
3. To reduce the number of litigations and the size of settlements associated with personnel having been exposed to health hazards when in the service of the Army and
4. To improve the selection of materiel alternatives.

The latter helps the materiel developer Army Materiel and Readiness Command (DARCOM) by comparing the relative hazards of alternative materials available for use. Such materials include chemicals, propellants that result in toxic exhaust or combustion products, intermediate chemicals used in the manufacture of items to which humans are exposed, etc.

Scope of Plan

The Plan reviews the types of tests that are needed, those that should be carried out at a new or a renovated facility and those extramurally, what facilities are available at two model organizations (Letterman Army Institute of Research (LAIR) and Hunters Point), conceptual designs for incorporating a Medical Research and Development Command (MRDC) selected capability and capacity, Army-unique exposures, services that could be provided to the Facility by the host Government agency,[a] the "new" Facility and purchased extramurally, and the continuous development of Army related toxicology requirements and adaption to changes in these requirements.

Approach

The approach utilized in preparing this Plan, was to view the new or MRDC added toxicology testing capacity from the science point of view. This is in contrast to the Management Plan, which views from the Facility a business orientation. The Plan preparation sequentially followed the identification of the Army's toxicology requirements, both regulatory and nonregulatory, options for meeting these requirements, an identification of the facility and equipment within the Facility, for carrying out a broad range of toxicology research/testing capabilities and modularized to provide a specified capacity (volume) of testing and technology development as a function of time, and the quality assurance activities needed to ensure the scientific credibility of the Facility's scientific/testing output.

Assumptions

The assumptions used include:

1. All science must be good quality for the research and test's purposes.

2. All regulation relating to conformance to Good Laboratory Practice (GLP) will be met.

3. All non-regulation research and testing will conform to the GLP and the protocols established (selected or developed). Some research/testing should not incorporate all the formal activities inherent in GLP regulations. An example would be an experiment carried out under The Surgeon General's non-regulatory responsibility which does not require extensive specimen or recordkeeping procedures nor establish a concise level of training or experience by the person carrying out the experiment or interpreting the results. The work, however, should always be good science.

(a) The expression "host Government organization" refers to the agency that would be occupying or managing the facility in which the added toxicology testing capability would be incorporated.

4. There will be both all Army and non-Army reviews of operating policies and performance.

5. There will be good Standard Operating Procedures (SOPs) developed by the scientists in coordination with the Quality Assurance function. (See Quality Assurance Plan, TR-477-17.) Such SOPs will provide, for example, the use of double blind sampling.

6. The technical operation will be headed by a Science Director who will control technical performance and employ technical tasking methods.

7. Data and recordkeeping will be given prominent attention. The data and record formats shall follow as appropriate, the National Cancer Institute guidelines. These formats allow data and records to be stored in the Carcinogenesis Bioassays Data System for computerized data collection, retrieval and analysis.

8. The facility and personnel will conform to the requirements for certification and accreditations for facilties and personnel. Appendix 2 contains a list of personnel and facility accreditations and certifications.

9. Personnel will be allowed the maximum for innovative methodology development consistent with the needs of the Army.

The purpose of this Plan is to ensure that the final Facility Specification and Personnel Position Descriptions provide the policies and guidelines that will result in the data and scientific output generated by personnel utilizing the Facility, are scientifically acceptable. Further, that technical personnel will be attracted to the Facility because of its reputation and qualifications of the scientific personnel working at the Facility.

Clarifications

The Plan developed as part of the Problem Definition Study covered mammalian toxicology research/testing but did not cover:

1. Basic Toxicology Research
2. Personnel Training
3. Full Service Toxicology Capability
4. Occupational Health Aspects
5. Health Hazard Assessment

Basic research and training are important portions of toxicology but were outside the scope of the study.

Training is a very important mission. It should be included in the new Facility capability. Toxicology related personnel will be in short supply for the next decade. An Army training program would be a cost-effective method for meeting the Army's toxicology needs of the future. The training should provide professionals the opportunity for a multifaceted, advanced Ph.D. degree program in toxicology. Further, the training program should also provide for training

middle and technician level staff. The purpose is to teach them how to effectively carry out the work to be done. Finally, the program should train inspectors. The laws and new perceived responsibility associated with toxic hazards require that this "new" Army position will have to have personnel trained for doing Army field work. They do not exist in the quantity needed.

Toxicology is a subset of Occupational Health, which is a subset of Health Hazard Assessment. The methodology used to evaluate the Army's requirements and approach to meeting its toxicology needs, therefore, serves as a model for addressing the more complex Occupational Health and Health Hazard Assessment requirements for the global Army.

The toxicology that was part of the Problem Definition Study related to health and not toxicology technology related to the environment. The Problem Definition Study covered mammalian toxicology testing and applied mammalian toxicology research. It did not, however, cover the toxicology services typically needed before the testing is initiated, in parallel with the testing or after the testing is completed. The services provided by a full service toxicology facility can be divided into:

a. Services provided on a continuing basis
b. Services provided as part of the task assignment

Appendix 3 and 4 contain lists of these full-service activities, respectively.

Facility Organization

The toxicology research/testing facility has been organized as shown in Figure 1. It includes six major business functions:

1. Administration
2. Financial
3. Legal/Contract Administration
4. Product/Quality Assurance (of which GLP is a subset)
5. Support Services
6. Toxicology Research/Testing

It should be noted that the organizational chart has been depicted as a Government-owned, contractor-operated (GOCO) facility. The result would be equally true if it was a Government-owned, Government-operated (GOGO) Facility or a contractor-owned, Government-operated (COGO) Facility.

Note, the Product/Quality Assurance function (of which Good Laboratory Practices) are a subset reports directly to the parent organization and only indirectly reports to the Manager of the Toxicology Facility. This is to ensure monitoring and enforcement of Product/Quality Assurance is soundly implemented.

Interrelations With Other Tasks

This Plan relates to the other six portions of the Facility's installation and operation: facility floor plans and construction, equipment, quality assurance, personnel, resources and management. Since this Plan interrelates with others,

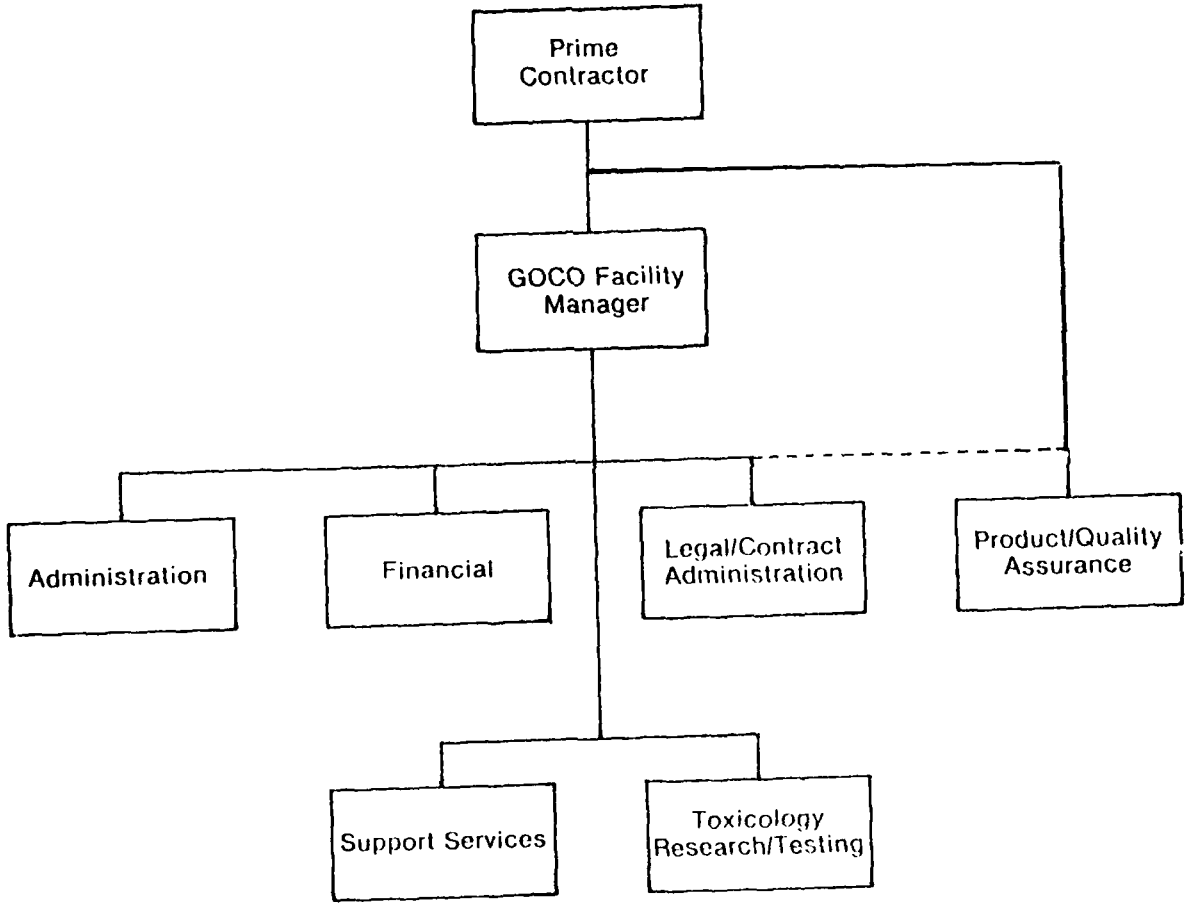


FIGURE 1 TOXICOLOGY TESTING FACILITY ORGANIZATION

certain duplication of subject material exists. Attempts have been made to minimize this at some penalty in the "self-contained" nature of the individual reports.

Total Capability

The Problem Definition Study did not provide for selecting the total capability to be incorporated into the Facility. The program's scope was limited to mammalian toxicology testing and, through a subsequent redefinition, to include applied mammalian toxicology research.

A full-service mammalian toxicology research testing facility would include services provided:

a. Before the testing was initiated,
b. The testing itself,
c. Activities carried out in parallel with testing and
d. Services after testing.

in the Basic Research and Training functions. Figure 2 illustrates this.

Appendix 3 contains an itemized listing of activities that could be considered routinely provided within a full service Applied Mammalian Toxicology Research/ Testing Facility.

Incorporated Capability

The actual capability incorporated must be decided by the MRDC Commander/Staff. As a minimum, it is recommended the Facility provide for:

a. Literature and information review/searches,
b. Consulting on the toxicology hazards associated with materiel and weapon probrams,
c. Consulting on needed regulatory compliance and
d. Actual mammalian toxicology research/testing through a minimum of four routes of exposure (oral, inhalation, dermal and ocular).

The last item noted a "minimum" of four routes of exposure. Many of the others such as surgical implantation, interdermal, intragastric, etc. should also be included. Appendix 5 provides a list of Routes of Administration/ Exposure.

Detailed Functional Organization and Associated Labs and Areas

Figure 3 presents a further breakdown of the types of toxicology science and organizational services included in a full-service capability. It reflects, for example, the difference between those supporting services considered a permanent part of the Facility and those which would be considered acquirable under a services cotract, level of effort contract or subcontract basis.

More information is presented on this later.

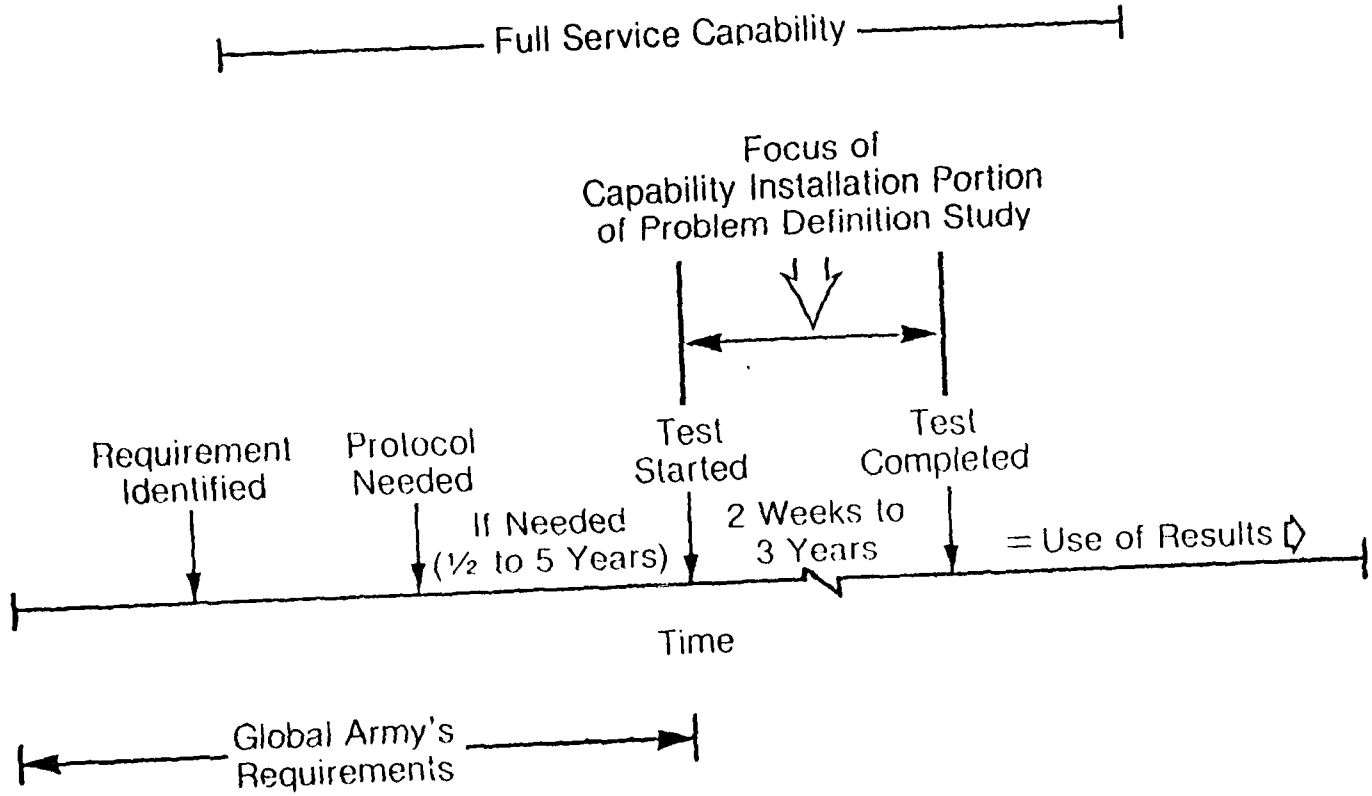


FIGURE 2 ILLUSTRATION OF FULL SERVICE CAPABILITY

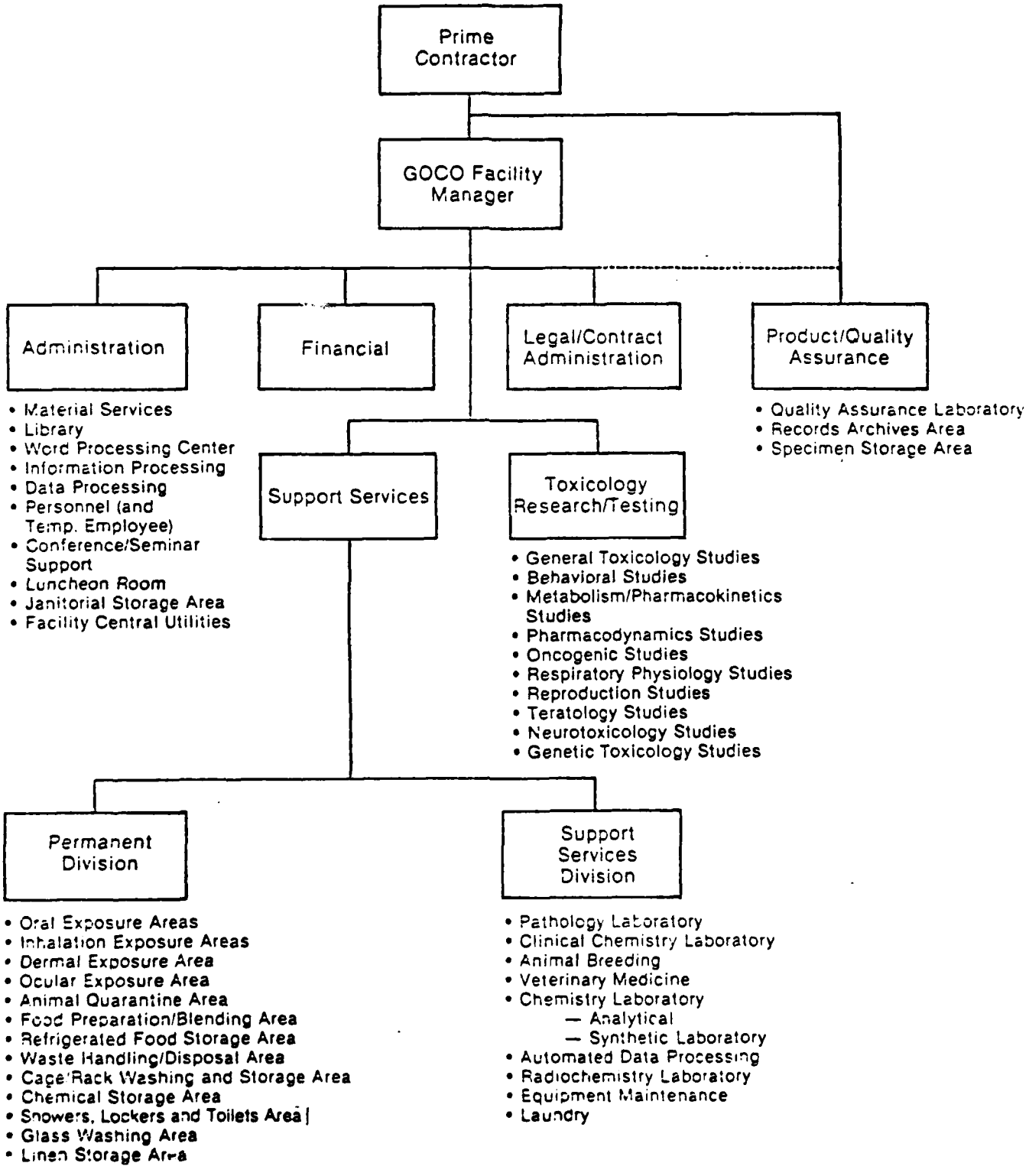


FIGURE 3 ORGANIZATIONAL LOCATION OF FACILITY LABS AND AREAS

REQUIREMENTS

The Problem Definition Study included evaluation of the global Army's requirements for mammalian toxicology. These requirements were evaluated from a full-service toxicology research/testing capability viewpoint. The requirements could also be subdivided into nonmedical and medical requirements. This was not done since the line separating the mission of the Army's medical and non-medical organizations was not clear to team members.

The added Army toxicology testing capability reflected by the Facility Plan discussed elsewhere, covers a portion of that portion of the Army's requirements typically expected to be provided by the MRDC.

Army's Business Environments

There are seven Army business environments which require toxicology technology:

1. Research, Development, Test and Engineering (RDT&E) (e.g., drug development)
2. Manufacturing (e.g., munitions)
3. Transporting (e.g., hazardous material)
4. Inventory (in-use and depot, e.g., storage and maintenance)
5. Combat training operations (e.g., smoke simulants)
6. Combat operations (e.g., chemical warfare)
7. Demilitarization (deactivation, disposal) (e.g., obsolete nerve gases)

Toxicology Requirements Volume

The total volume of the Army's toxicology requirements is a function of at least three parameters:

a. The specific item of material,
b. The stage in its life cycle (research through demilitarization) and
c. That (those) portion(s) of the full-service toxicology capability involved.

To arrive at a total for the volume of Army toxicology requirements, therefore, requires each item and occasionally, categories of Army materiel to be viewed at each stage in its life cycle, for the need for toxicology capability (any? to how many?). This is a tremendously large undertaking. It involves the monumental task of identifying all the materiel within the Army's RDT&E process and inventory; evaluating each for toxic hazards; etc. (Many of the items in inventory were put there years ago, before the toxic hazards associated with many chemical substances was known.)

A finalized itemization, therefore, of the total volume of Army toxicology requirements could not be completed within the program's scope and time frame. A major advance was made, however, in defining the scope of the toxicology requirements and to identify requirements to at least nine levels of five major Army materiel categories:

1. Aircraft (and Related Equipment)
2. Missiles (and Related Equipment)
3. Weapons and Tracked Combat Vehicles
4. Ammunition
5. Other Materiel

Further discussions of these requirements are contained in the program's "Comparative Analysis Report," TR-477-2.

The total volume of toxicology requirements results from specifically evaluating Army materiel items at stages in the life cycle and then according to which tasks of the full-service capability (Appendices 3 and 4) apply. The latter includes maintenance of the toxicology data bases during the 20 to 40 year life cycle of most Army materiel and testifying in front of regulatory agencies as expert witnesses at trials.

Requirements Define Tests

Reviewing the total Army requirements for toxicology services, resulted in a definition of the most likely mammalian toxicology tests needed. Some or all of these must be included in the added capability. This added capability, however, can be incorporated into any one or more of the various sources the Army has for meeting its toxic requirements. The latter are shown in Figure 4 and include:

1. In-house laboratories;
    a. Army Medical Department (AMED)
    b. DARCOM
2. Extravurally laboratories for hire:
    a. For profit
    b. Not for profit
    c. Universities
3. Other Government agencies:
    a. National Toxicology Program
    b. EPA, NIOSH
    c. NCTR
4. Industrial materiel developers
5. Chemical manufacturers

TYPE OF TESTS

Meeting the Army's toxicology requirements resulted in the identification of three categories of tests:

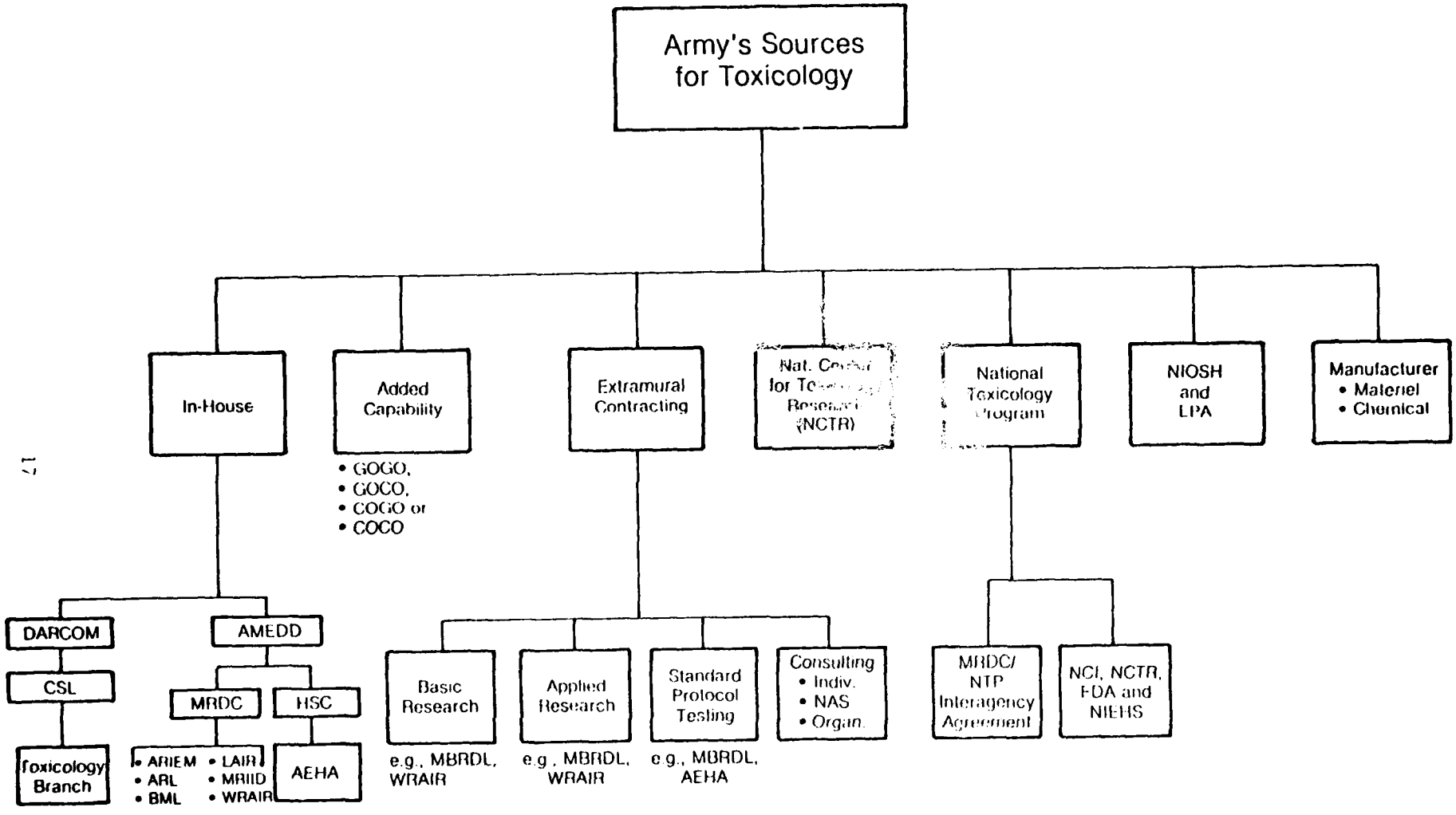


FIGURE 4 AVAILABLE SOURCES FOR ARMY'S TOXICOLOGY

1. General toxicology tests
2. Special scientific toxicology tests (studies)[a]
3. Genetic toxicology tests

General Toxicology Tests

Table 1 presents a list of 19 types of Army mammalian toxicology tests. Information on each tests includes duration, type of animal, route of exposure and outcome, usually "general toxicology." The later includes lethality, metabolism/pharmacokinetics and portions of service toxicology disciplines such as pharmacodynamics. Only portions, however, so as not be be confused with the full scale, special scientific studies. Also, General Toxicology, as used in this context, includes the dermal and ocular irritation and sensitization outcomes.

The list of 19 tests resulted from a survey of all known types of mammalian toxicology tests descriptors and reducing the list to those most likely to be applicable to the Army's requirements. This was followed by an identification of specific tests (protocols) which resulted in the group of 19.

To accomplish all the Army's mammalian toxicology research needs required that various special scientific toxicology tests be incorporated beyond the general toxicology tests and beyond the neurotoxicology tests (Table 1).

Special Scientific Toxicology Studies

The toxicology research/testing capability envisioned as able to be incorporated into the Facility include the follwoing:

1. Behavioral Studies
2. Metabolism/Pharmacokinetic Studies
3. Pharmacodynamic Studies
4. Oncogenic Studies
5. Respiratory Physiology Studies
6. Reproduction Studies
7. Teratology Studies
8. Neurotoxicity Studies

These are in addition to the General Toxicology tests cited in the prior section.

Of these, it is recommended the Facility provide the specific special toxicity studies noted at the right hand side of Table 2 including the combined protocols of (a) general toxicity and oncogenic studies and (b) reproduction and teratology studies. These include, for example, behavioral toxicity studies with rodents and primates and the inhalation route of exposure.

(a) For the remainder of the report, the special scientific toxicology tests will be referred to as studies. This is done to reflect the more research oriented aspect of the activities.

TABLE 1 SPECIFIC TYPES OF ARMY MAMMALIAN TOXICOLOGY TESTS

No.	Duration		Type of Animal	Route of Exposure	No. of Species	Outcome[a,b]
	General	Specific				
1.	Acute	Short	Rodent	Oral	1	General Toxicology
2.	Subchronic	90-Day	Rodent	Oral	1	General Toxicology
3.	Chronic	Life-Time	Rodent	Oral	1	General Toxicology
4.	Acute	Short	Rodent	Inhalation	1	General Toxicology
5.	Subchronic	X-Day	Rodent	Inhalation	1	General Toxicology
6.	Chronic	Life-Time	Rodent	Inhalation	1	General Toxicology
7.	Acute	Short	Primate	Inhalation	1	General Toxicology
8.	Subchronic	90-Day	Primate	Inhalation	1	General Toxicology
9.	Chronic	Life-Time	Primate	Inhalation	1	General Toxicology
10.	Subchronic	90-Day	Dog	Oral	1	General Toxicology
11.	Acute	Short	Rabbit	Dermal	1	General Toxicology
12.	Subchronic	Z-Day	Rabbit	Dermal	1	General Toxicology
13.	Acute	Short	Rabbit	Ocular	1	General Toxicology
14.	Acute	≥21 day	Chicken	Oral	1	Neurotoxicity
15.	Subchronic	90-day	Chicken	Oral	1	Neurotoxicity
16.	Acute	Short	Rabbit	Dermal	1	Irritation
17.	Subchronic	90-day	Rabbit	Dermal	1	Irritation
18.	Acute	Z-Day	Rabbit	Ocular	1	Irritation
19.	Acute	Short	Rodent[c]	Dermal	1	Sensitization

(a) Efficacy would be included for drugs and vaccines.
(b) General toxicology includes lethality and metabolism/pharmacokinetics plus minor investigations of the several other toxicology disciplines (e.g., pharmacodynamics).
(c) Guinea Pig

TABLE 2 MAMMALIAN TOXICOLOGY TEST PRICE LIST (3/8/81)

Test No.	Duration	Type of Animal	Route of Exposure	Price, $(000) Per Outcome[a]							
					Special Scientific Toxicology Studies[b]						
										Combined Protocols	
				General Toxicology[c]	Behavioral	Onco-genic	Repro-duction	Terato-genic	Neuro-toxi-cology	Gen. Tox. + Oncog.	Repro. Terato.
1	Acute	Rodent[d]	Oral	2.4[e]	—	—	—	—	—	—	—
2	Subchronic	Rodent[d]	Oral	56[e]	—	—	—	—	—	—	—
3	Chronic	Rodent[d]	Oral	495[e]	—	377[e]	114[e]	27[e]	—	600[f]	125[f]
4	Acute	Rodent[d]	Inhalation	5.0[e]	—	—	—	—	—	—	—
5	Subchronic	Rodent[d]	Inhalation	64[e]	100[f]	—	—	—	—	—	—
6	Chronic	Rodent[d]	Inhalation	613[e]	—	515[f]	—	—	—	1000[f]	—
7	Acute	Primate	Inhalation	39[f]	—	—	—	—	—	—	—
8	Subchronic	Primate	Inhalation	196[f]	150[f]	—	—	—	—	—	—
9	Chronic	Primate	Inhalation	518[f]	—	420[f]	—	—	—	800[f]	—
10	Subchronic	Dog	Oral	104[e]	—	—	—	—	—	—	—
11	Acute	Rabbit	Dermal	4.2[e]	—	—	—	—	—	—	—
12	Subchronic	Rabbit	Dermal	75[g]	—	—	—	—	—	—	—
13	Acute	Rabbit	Ocular	2.5[f]	—	—	—	—	—	—	—
14	Acute	Chicken	Oral	—	—	—	—	—	5.4[e]	—	—
15	Subchronic	Chicken	Oral	—	—	—	—	—	20[e]	—	—
				Irritation	Sensitization						
16	Acute	Rabbit	Dermal	0.7[e]	—						
17	Subchronic	Rabbit	Dermal	3.0[g]	—						
18	Acute	Rabbit	Ocular	0.9[e]	—						
19	Acute	Guinea Pig	Dermal	—	3.9[e]						

(a) Rounded off to nearest $1,000 for prices in excess of $5,000. Assumes one species.
(b) Special Scientific Toxicology Studies. Metabolism/Pharmacokinetics, Pharmacodynamics, and Respiratory are deleted since they are not a part of the 19 tests.
(c) General Toxicology includes lethality, metabolism and pharmacokinetics/pharmocodynamics.
(d) Rodent studies price was based on use of the rat.
(e) SOURCE: Enviro Control, Inc. 1980, Cost Analysis Methodology & Protocol Estimates. TSCA Health Standards and FIFRA Guidelines. Rockville, MD: Enviro Control, Inc. U.S. Environmental Protection Agency.
(f) Price estimated by LSI since no quotable source was identified.
(g) SOURCE: ICF, Inc. 1980. Profile of the Chemical Safety Testing Industry: An Assessment of Pesticide Testing Capacity. Final Report. Washington, DC. ICF, Inc. U.S. Environmental Protection Agency.

TABLE 3 GENETIC TOXICOLOGY TESTS

A. Standards for Detecting Gene Mutations

1. Detection of Gene Mutations in Bacteria
   a. The Salmonella/Microsomal Assay
   b. The Escherichia coli WP2 and WP2 *uvrA* Reverse Mutation Assay
2. Detection of Gene Mutations in Eukaryotic Microorganisms
   a. Aspergillus nidulans
   b. *Neurospora crassa*
3. Detection of Gene Mutations in Insects
   a. Drosophila melanogaster Sex-Linked Recessive Lethal Test
4. Detection of Gene Mutations in Somatic Cells in Culture
   a. Mammalian Cell Culture — L5178Y Mouse Lymphoma Cells
   b. Mammalian Cell Culture — V79 Chinese Hamster Cells
   c. Mammalian Cell Culture — Chinese Hamster Ovary (CHO) Cells
5. Detection of Gene Mutations in Mammals
   a. The Mouse Specific Locus Test

B. Standards for Detecting Heritable Chromosomal Mutations

1. In Vivo Cytogentics Test in Mammals
2. Detection of Heritable Chromosomal Damage in Insects
   a. Chromosomal Damage in Drosophila melanogaster
3. The Dominant Lethal Test in Mammals
4. The Heritable Translocation Assay

C. Standards for Detecting DNA Repair or Recombination as an Indicator of Genetic Damage

1. Detection of Genetic Damage in Bacterial by DNA Repair
2. Unscheduled DNA Synthesis in Mammalian Cells in Culture
3. Detection of Mitotic Crossing Over and/or Gene Conversion in Yeast
4. Sister Chromated Exchange in Mammalian Cells in Culture

D. Standards for Detecting Chromosomal Damage

1. In Vitro Cytogenetics Assay
2. Micronucleus Assay

E. Standards for Detecting DNA Alkylation

1. DNA Alkylation in Drosophila melanogaster Sperm Cells
2. DNA Alkylation in Rodent Sperm Cells
3. DNA Alkylation in Mammalian Cells in Culture

Table 2 lists the price established for the various mammalian toxicology tests where they could be done on a contracted basis. Obtaining pricing information for toxicology testing is very difficult. This resutls because of the inconsistencies in protocols, interpretation of protocols, depth with which the personnel providing pricing information views the assignment, etc. The table is included, however, more to reflect the breakout of tests the Facility should perform to meet Army requirements than the price for the test. The background discussions on the latter are contained in the program file Memo.

Genetic Toxicology Tests

Considerable advances in technology are being made to minimize the cost of toxicology testing. A portion of these efforts involve genetic toxicology tests. The program identified five major genetic toxicology test categories:

1. Standards for detecting gene mutations;
2. Standards for detecting heritable chromosomal mutations;
3. Standards for detecting DNA repair or recombination as an indicator of genetic damage;
4. Standards for detecting chromosomal damage; and
5. Standards for detecting DNA alkylation.

These five tests categories are further defined in Table 3.

It is the Army's decision as to which of the genetic toxicology tests be incorporated into the Facility's capability. It is recommended that many of the in vitro tests be included (Module 62). The in vivo genetic toxicology studies, can be incorporated through the addition of Module 63 or, with some rearrangement, through one of the oral exposure areas (e.g., Modules 1 through 3, acute, subchronic and chronic oral exposure areas for rodents, respectively).

Tests Actually Selected

A specific selection of which capabilities/mammalian toxicology tests should be done within the Facility depends upon decisions made concerning:

1. The control the Army desires over the implementation of each test;
2. The level of funding it desires to invest in establishing the Facility, its capability and capacity; and
3. The success experienced in identifying the level of test volume, urgency and timing for providing the capability.

A major driver will be the number of times (volume) the particular test is ultimately determined to be required, the funding provided by the Facility users and, possibly, the sharing of the Facility capabilities with other organizations. The latter includes the Air Force and Navy, and other Federal Agencies such as the National Cancer Institute or other National Toxicology Program participating agencies.

IMPLEMENTING SELECTED CAPABILITY AT THE FACILITY

As was noted the specific tests and toxicology related activities/tasks incorporated must be determined by the Army. It is envisioned, however, that the

selected capability should be implemented in two stages. Further, each stage should be built up incrementally.

Two Stages

The capability selected by the decision-makers for the Facility should be divided into two parts:

1. The initial capability
2. The growth capability

Initial Capability

The initial capability should be a balance between priority requirements and the available resources (dollars and personnel, and to a more limited extent facilities and equipment). The time frame should be the first five years of the Facility's existance. These five years include:

1. Final definition of the Facility Specification, including capability and capacity decisions, operating policy and guideline decisions, etc.

2. Approved detailed Facility drawings, the subsequent construction and, then turning it over to the operator.

3. Initial startup of toxicology testing, easier ones first.

4. Fully operational initial capability.

Growth Capability

The growth capability should be selected and conceptually designed at the time the initial capability is formalized. Details of its configuration however, should not be formalized until after the third year of the initial capability's "existance."

The purpose of conceptually defining the growth capability along with finalizing the initial capability, is to ensure the capability, floor plans, equipment and personnel are compatible, to alert potential users and the facility staff as to what is coming in the future, and to aid in explaining why it is not incorporated initially.

Incremental Buildup in Each Stage

For a variety of reasons, including effective management of resources and the acquisition of personnel, the facility should have its capability incorporated into the Facility in a step-wise fashion. This will avoid having too many "new" things going on simultaneously. It will allow management, both scientific and business, more time to develop, implement, and teach and/or acquire the operating procedures, guidelines, policies, personnel, etc. that make up the Facility.

Preferred Tests at New Facility

Above it was noted the full service capability that was conceptually designed for the Facility. Further, it was noted that not all should be incorporated either initially of in the growth version. Many ways can be envisioned for selecting the capability to be included. The following illustrates some.

Army-Unique Exposures

No major toxicology research/testing capability exists able to handle all the routes of exposure that reflect the Army's requirements. These include:

1. Troop exposures associated with weapons systems.
2. Industrial workers in Government-owned plants and Army depots where Army-unique chemicals or materiel are made or processed.
3. Environmental exposures the general public experiences when living near Army activities. These include exposure to Army "generated" air, water and toxic wastes.

An example is the soldier exposed to a short-term, very intense concentration of weapon "exhausts" with concommitant stress conditions such as noise, vibration, strees, etc. The latter are described in more detail later.

Not Competitively Available Extramurally

A second category of tests that should be given high priority for initial incorporation into the Facility include those that cannot be obtained extramurally on a competitive basis. The caution, however, is that the volume of these second priority tests be adequate to justify their incorporation into the Facility's capability.

The incorporation of a behavioral toxicology capability represents the type of tests that can not be obtained extramurally through a broad base of competition. Further, the trend in toxicology is toward evaluating the effect on behavior of concommitant exposure conditions (temperature, noise, physiological state, radiation, etc.). This aspect of technology is similar to the Army's need for evaluating the soldier's exposure to toxic chemicals and hazards and/or military-unique environment. Behavioral toxicology, however, cannot be justified during the initial capability because of the higher demand of the more traditional toxicology research/testing.

Tier Tests

In Tables 1 and 2 the tests were identified as acute, subchronic and chronic tests. They were examined as if they were a discrete entity which, insofar as being specific tests to make specific determinations, they are. In reality, however, the assessment of a product or process, new or old, will include examination of several and, in extreme cases, all of the tabulated effects. This means that in practice most toxicological testing will be subject to a battery of tests (Dominguez 1979, p. 116).(1)

(1) References are cited at the end of the report.

These battery of tests may be based on the type of effect, duration (acute, subchronic or chronic), or may involve one design to determine one particular effect, such as carcinogenicity the Special Scientific Toxicology Tests discussed above. The latter case may take the form of a progression from the least expensive and most expedient screening procedure to the more expensive and time-consuming lifetime study. This can be exemplified from the Ames test to full-scale two-year animal feeding.

At other times it is the tests reliability that may be the problem -- mutagenicity testing by in vitro techniques where more than one procedure increases the reliability of results and their extrapolatability. Whichever is the case, the implication for a Technical Plan is the same, a series of tests must be developed relating to the testing objective.

The situation, however, is further complicated in that the testing program design must also take into consideration several additional factors if it is to be realistic and cost-effective. The basic parameters usually employed in designing testing systems are:

1. The opportunity for exposure, frequency, duration, concentration and route.

2. The nature of the hazard being evaluated -- acute, subchronic or chronic effects.

3. The volume of the material or materiel to be produced. In general, the larger the volume produced the greater potential for human or environmental exposure and the greater need for most extensive testing. (This, obviously, is not always the case since consideration of points mentioned in items 1 and 6 may mitigate.)

4. The physical and chemical properties of the substance. It is illogical and unnecessary, for example, to conduct inhalation studies on a nonvolatile material.

5. The structural activity relationships of the substances under consideration to other tested substances and their known effects. Certain preliminary inferences can be drawn based on such analogies. As more experienced knowledge grows, it may be possible to use this approach more definitively.

6. The known or anticipated uses of the substances. This plays a large part in the intelligent design of a testing system for specific tests. It is unnecessary, for example, to conduct extensive, if any, tests on a substances formed and totally consumed in the reaction of another substance, for instance, a transient reaction product. At the other end of the spectrum, however, is a product intended for wide-spread use within the Army which would warrant extensive evaluation. The latter could depend upon the nature of the Army personnel's use or dictates of legal statutes.

These six factors have ignored statutory or regulatory requirements but view testing from the most logical and scientific viewpoints. The implications raised by laws or regulations, TSCA, FIFRA, DOD, OSHA, etc., although beyond the scope of this report, are, obviously, instrumental in final test system design.

Table 4 presents a summary of three levels of tier testing guidelines (Dominguez 1979, p. 120) modified for this program. A level called tier zero covers such items as physical/chemical properties, elementary mass balance analysis and preliminary analytical methods determination.

The trend is toward increased complexity and resources (cost, facilities, equipment and personnel) as one goes from tier one through tier three tests.

Projected Shortages of Mammalian Toxicology Testing

The national capability for applied mammalian toxicology research/testing will be limited (ICF, Inc. 1980; Development Planning and Research Associates, Inc. and FCF, Inc. 1980). The ability of the Army to compete effectively for extramural toxicology research/testing has certain restrictions placed on it. These are summarized in Table 5 as they relate to the projected supply and demand for five particular categories:

1. Personnel
2. Facilities
3. Equipment
4. Animals
5. Business Profit

To illustrate, personnel involved with mammalian toxicology research/testing will be in low supply and the demand will be high because of the recent increase in regulatory actions and public/business awareness of the hazards associated with chemicals. The Army's need for personnel further restricts the supply because of the special training needed for Army exposures, the nonmedical war image versus a "peace" image and the Army's greater requirement for production type testing than the more interesting (to the toxicology scientist), basic and applied research. These drivers on personnel, facilities, equipment, animals and business profit must be considered when selecting the particular capabilities to be incorporated into the Facility.

RECOMMENDED EXTRAMURAL TESTING

The extramural testing done under contract or through an outside Federal agency can be broken down into:

1. The characteristics of the test.
2. The service portion of the tests.

Characteristics of Extramural Tests

The test that should be carried out external to the Facility's capability include:

TABLE 4 PROGRAM TIER TESTING GUIDELINES[a]

TIER 0

- Physical/Chemical Properties
- Elementary Mass Balance Analysis
- Preliminary Analytical Methods

TIER I

- Acute General[b] Toxicity Tests
- Genetic Toxicity Tests for Chronic Health Effects
- Refinement and Application of Analytical Procedures

TIER II

- Subchronic General Toxicity Tests
- Reproduction and Teratogenicity Tests
- Neurotoxicity and Behavioral Toxicity
- Further Refinement and Application of Analytical Methods

TIER III

- Chronic General Toxicity Tests
- Oncogenicity Tests
- Further Refinement and Application of Analytical Methods

(a) Based on approaches for developing testing guidelines under the Toxic Substances Control Act—June, 1978. This approach is a modification of that developed by panelists under the auspices of The Conservation Foundation.

(b) General toxicity tests may include metabolism, pharmacokinetics/pharmacodynamics and respiratory physiology studies.

TABLE 5 CATEGORIES USED TO PROJECT SHORTAGE OF AMTR CAPABILITIES

	Drivers		
Category	Supply	Demand	Army's Restriction
• Personnel	Low	High	Needs special training, program's not basic (more interesting) research, war versus peaceful
• Facilities	Low		Must meet highly hazardous safety criteria
• Equipment	Low		Must provide unique durations and high concentrations of hard to reproduce environments
• Animals	Low on Primate		Against doing testing on dogs.
• Business (Profit)	Small	High	Low fees on contracts (10 vs. 25%), unique material, environments, scheduling, "red tape", etc.

1. Tests already being completed within the MRDC's laboratories.

2. Tests which such organizations as the National Toxicology Program, EPA, NIOSH, etc., would provide (limited opportunity for Army requirements in general but still a viable option).

3. Tests characterized by using very routine, standard protocols.

4. Tests where competitively meaningful numbers of for-hire laboratories provide quality type testing.

5. Tests for requirements where the time available to obtain the results is long and the quick response, characteristic of a Government-owned and Government controlled operation through its own staff or that of a contractor.

Service Portions of Test

As was indicated in Figure 3, various support services were identified in a Support Services Division. These included:

1. Pathology Laboratory
2. Clinical Chemistry Laboratory
3. Animal Breeding
4. Veterinary Medicine
5. Analytical and Synthetic Chemistry Laboratory
6. Automated Data Processsing
7. Radiochemistry Laboratory
8. Equipment Maintenance (servicing and repair)
9. Laundry

The selection of which services to purchase extramurally is judgemental. It is based upon preferred rate of buildup in testing capacity, availability of personnel hired for staffing the new Facility, etc. These issues are discussed in more detail later.

FACILITY

The program specified several models as sites for adding to the Army's applied mammalian toxicology research/testing capability. The Facility sites were:

1. LAIR
2. Hunters Point

Site Models

To a degree, the two models utilized represent extremes in potential Army facilities for locating the toxicology Facility. The LAIR represents a modern (four to eight years old), functioning facility. Hunters Point represents an obsolete (>25 years old), dormant facility.

LAIR Restrictions

The Facility Plan reviews in detail the deficiencies of the LAIR facility. Major among them are the need for renovation work while the existing activities continue; inadequate capacity of many business utilities for a modern, GLP qualifiable Facility and several minor structural arrangements which make capability module layout difficult.

None of the restrictions found with LAIR, however, inhibit it from becoming an effective structure/facility to incorporated the mammalian toxicology testing research capability selected to be added.

Hunters Point Restrictions

The Facility Plan reviews in detail the deficiencies of the Hunters Point facility. Among them are the poor state of the property, the considerable repair needed (e.g., most of the facility's central utilities will have to be replaced) and the lack of any host Government organization services. The structural arrangement, however, is better than LAIR's.

Resources Needed Proportional to Capability and Capacity

The Facility's resource needs are directly related to that portion of the global Army's requirements for toxicology capability to be included in the Facility. Further, the needs are then related to the type of capability (scientific and testing) and capacity that are selected for incorporation into the facility. Capacity refers to rate of experimentation or testing per unit of time. Resources refer to area of facility, equipment, personnel, money, reputation, etc.

Capability

As noted in Tables 1 and 2, 19 specific tests were identified as needed to meet the Army's requirements plus the special scientific and genetic research efforts and tests.

It was not appropriate for the Problem Definition Study team to select the final capability to be included in the Facility. This relates to and is determined by MRDC's/DA's preferences, priorities, resources, timing, etc.

Capacity

The capacity is a function of the number of tests or amount of research done per unit time. As expected, capacity relates to the number of modules of a given capability or service (e.g., subchronic inhalation exposure areas for rodents or analytical chemistry laboratory), the number of personnel available to carry out the tests or experiments (e.g., animal caretakers) and to interpret the results (e.g., veterinarian pathologist), funding available for expendables, overhead, etc. Again, the final selection of Facility's capacity is a MRDC/DA decision.

Equipment Limitations

Two major limitations for any Army site selected for locating the Facility include:

1. The nonexistance of adequate or in most cases, any inhalation exposure areas.
2. The nonexistance of any Army-unique exposure chambers.

Inhalation Exposure Areas

Inhalation exposure is continuously being recognized as one of the more important but less availble toxicology routes of exposure. Many, if not the greater portion, of the Army's requirements are associated with inhalation exposures. This results from the combat and combat training operating environments Army personnel encounter (smokes and obscurants systems, the exhausts of weapons, the exhaust of large quantities of mobile equipment, protection against chemical warfare agent environments, etc.). This makes the addition of inhalation exposure areas a high priority for incorporation into the Facility.

Army-Unique Chambers and Toxic Chemicals/Generators

As discussed in more detail below, the Army has a variety of very unique exposure environments. These require unique chambers to simulate the exposure as well as equipment to generate a duplicate of the field exposure in the laboratory. The Army had one of the largest needs, for example for inhalation toxicology testing associated with aerosols. These result from soldier exposure scenarios involving offensive and defensive warfare agents, smokes and obscurants, etc. The capability added to the Facility must develop and then provide these unique chambers and generators to simulate the Army-unique environments.

CONCEPTUAL DESIGN RELATES TO CAPABILITY AND CAPACITY INCORPORATED

The technical design is a function of capability and capacity incorporated.

Conceptual Designs of Equipment and Facility Modules

The Problem Definition Study did not cover the development of a full service capability to meet all Army's requirements. The approach selected, therefore, was to design a total capability from a conceptual point of view able to meet all requirements. The actual capabilities and capacities incorporated into the Facility being a function of the MRDC Commander/Staff decision-making process.

Facility Modules

The full-service applied research/testing capability was conceptualized as modules. (See discussion in Facility Plan Report, TR-477-22.) The conceptual capability includes special modules to be used by various toxicology scientific disciplines to carry out the Special Scientific Toxicology Studies and Genetic Toxicology Tests. Appendix 6 contains a list of all the research/testing facility areas and laboratories. Appendix 7 contains three examples of the Mammalian Toxicology Facility Module Descriptions, Form 650. These forms contain information on:

1. Floor plan
2. Construction information
3. Special feastures/benefits
4. Special assumptions
5. Cost estimate

The examples presented in Appendix 7 are those for the Rodent Acute Inhalation Exposure Area, the Primate Subchronic Inhalation Exposure Area and the Pathology Laboratory, modules 1, 9 and 25, respectively.

LAIR Floor Plan

Appendix 8 provides the floor plans of the LAIR facility. It identifies the approximately 325,000 square feet space that was specified by the Army as being the maximum available for the Facility. The remainder is occupied by the U.S. Department of Agriculture and has been marked off on the floor plans. The expression AS stands for Administration Sections, LR for Laboratory Research section and RS for the Research Section. Realistically, the current DRDC related LAIR mission activities occupy a portion of this 325,000 square feet of "maximum space available." It is projected that less than 200,000 square feet of space will be available for the new Facility.

Equipment

Equipment lists were assembled for each of the Facility's capability modules. They are done in more detail in the "Equipment Plan Report," TR-477-21.

Special Scientific Toxicology Studies

Module numbers 13 through 19 and 61 are Special Scientific Toxicology Studies Areas. They provide for studies associated with the following toxicology disciplines:

1. Module 13, Behavioral Studies Areas
2. Module 14, Metabolism/Pharmacokinetics Studies Areas
3. Module 15, Pharmacodynamics Studies Areas
4. Module 16, Oncogenic Studies Areas
5. Module 17, Respiratory Physiology Studies Areas
6. Module 18, Reproduction Studies Areas
7. Module 19, Teratology Studies Areas
8. Module 61, Neurotoxicology Studies Areas

Certainly not all these study areas will be incorporated in the growth capability much less the initial capability. Judgement will have to be made concerning what are the Army's priorities. The initial capability, however, will start with General Toxicology as its primary thrust.

Model Facility Locations

As noted, LAIR and Hunters Point served as models to depict potential sites for incorporating the added capability. Both sites were viewed from the ability to be converted into high quality, scientific institutes of toxicology. Both facilities being located in the San Francisco CA area, have ready access

to personnel, local universities focusing on toxicology work (e.g., University of California at Davis) and local sources for analytical laboratories, technicians, pathology laboratories, etc.

The LAIR, with its location at the base of the Golden Gate Bridge is a most attractive site. The Facility is the more modern. Hunters Point will require extensive rework in and around the facility to convert it into an Army or medical institute of toxicology, MRDC center of toxicology testing or location for additional MRDC mammalian toxicology testing.

ARMY-UNIQUE EXPOSURES

By nature of its mission, the Army exposes its military and civilian personnel to unique toxic exposures. The most unique are those associated with the combat or combat training environments. These are characterized as shown in Table 6. As the table indicates, the exposure is short-term (less than one minute to one hour, repeated exposures of one to sixty times per ten hour day, etc.).

The characteristic called "intense concentration" deserves special mention. It reflects that the concentration of chemicals, chemical mixtures, exhaust gases, etc. is high in the combat environment or simulated combat environments. Such environments can occur from rapid firing of small arms to periodic missile launches, the generation of smokes to obscure the activities associated with troop and equipment movement, the exposure to chemical and biological warfare agents, etc.

Example

Figure 5 presents typical data of concentrations versus time for an armored vehicle undergoing a chemical agent challenge test. Such a vehicle would be the M1, Abrams Main Battle Tank. Although the time axis is left general, the impact of the unique environment is presented.

Concommitant Exposures

An area that will require increasing Army emphasis during the 1980s is the impact on soldier performance when exposed to toxic chemicals and environments and simultaneously exposed to such concommitant exposures as hot and cold temperatures, loud and intermittent noises, vibration, intermittent shock at various levels, etc. These exposures are summarized in Table 7.

SERVICES THAT COULD BE PROVIDED TO THE FACILITY

There are three sources of services available to or at the Facility. These include:

1. Host Government Facility Services
2. New Facility Services
3. Externally Purchased Services

Appendix 8 presents a list of 246 business services that could be provided-from-or purchased-for-the-Facility. They have been coded to include those which

TABLE 6 ARMY UNIQUE EXPOSURE SCENARIO

Characteristic	Level
Short Term Exposure	<1 min. to 1 hr.
Repeated Exposure	1 to 60 times/10 hr. day
Intermittent Exposure Frequencies	1 day/week to 90 days continuous
Intense Concentration	Above existing ceilings
Unique Environmental Conditions	
Temperature	−40 to 140 F
Relative Humidity	10 to 100%
Ambient Pressure	See Level to that at 8,000 ft
Associated Stress Conditions	
Noise	Loud, Sporatic
Vibration	Constant, but Varying
Shock	Periodic, Intense
Overpressures	Blasts, Shock Waves
Psycological	Stress, Threats

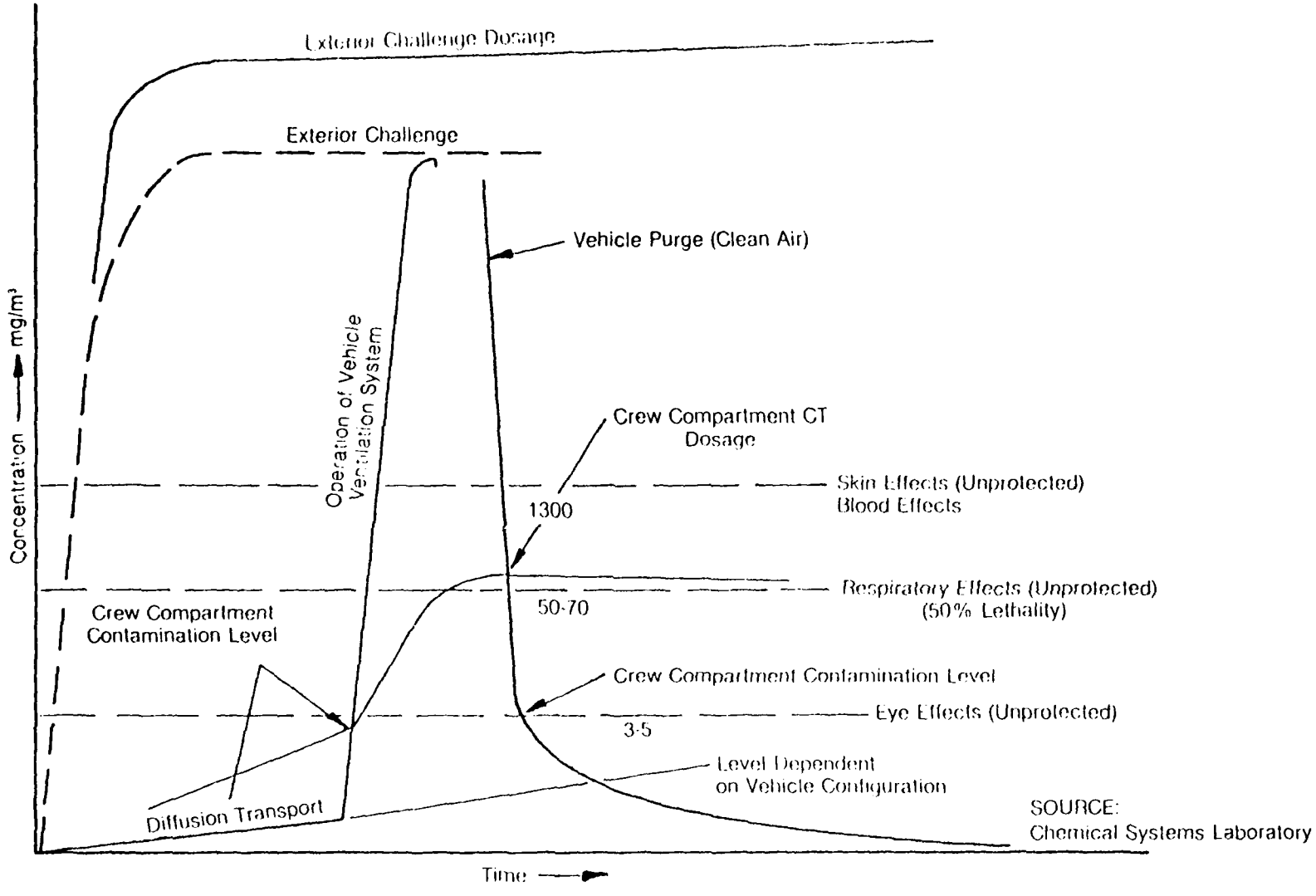


FIGURE 5 TYPICAL ARMORED VEHICLE CHALLENGE TESTING DATA

TABLE 7 CONCOMMITANT EXPOSURES THAT WILL MODIFY STANDARD TOXICOLOGY TESTS

Temperature	Hot / Cold
Noise	Loud / Nonauditory, Intermittent and Continuous
Vibration	Continuous, Peaks
Shock	Periodic, Intense
G-Forces	None / ??
Over-pressures	Blasts, Shock Waves
Relative Humidity	Dry / Wet
Visibility	Light / Dark; Fog / Rain / Snow
Ambient Pressures	Mountain
Pyscological State	Stressful (Threatening, Uncertain), Neuropsychiatric
Radiation	Ionizing / Nonionizing

should be given serious consideration (total of 40) and those which would be considered good candidates for consideration (total of 39). Final selection depends upon MRDC's/DA's priorities, resources, requirements addressed and capabilities and capacity incorporated.

Government Facility Services

The facility services that the host government organization would provide will depend upon the site selected as the two models used in the study indicated.

LAIR Facility Services

As an Army program guideline, the LAIR was assumed to provide no facilities. It is known, however, the LAIR can provide animal, laboratory, administrative and storage space on an as available/as needed basis. In addition, certain amounts of heating and air conditioning, electricity, tap water, sewage treatment, telephone system, compressed air in laboratory gases, general building maintenance and janitorial services could be available. Final selection is an open item at this time.

Hunters Point Services

Hunters Point has virtually no services available. The building has been "in mothballs" so no current people-provided-service exist. Also most of the central facilities are in a state of disrepair.

The Facility Services

Figure 3 presented a listing of those facility services considered for incorporation into the baseline capability and would then be available to the host organization. These included:

1. Oral, Inhalation, Dermal and Ocular Exposure Areas.
2. Animal Quarantine Area.
3. Food Preparation/Blending Area.
4. Refrigerated Food Storage Area.
5. Weight Handling/Disposal Area.
6. Cage/Rack Washing and Storage Area.
7. Chemical Storage Area.
8. Showers, Lockers and Toilet Area.
9. Glass Washing Area.
10. Linen Storage Area.

As can be seen, the areas vary from the testing exposure areas to storage areas.

Extramurally Purchased Services

Besides the support services recommended for purchasing outside mentioned previously, Figure 3, Support Services Division services, others that could be considered include: photography service, janitorial service, machine shop services, refuse pickup/disposal, etc.

Support service contracts could also be viewed as appropriate additions to a Technical Plan. These contracts provide, for example, the hiring of:

1. Animal handling people.
2. Animal care people.
3. Animal husbandry people.
4. Computer services people.
5. Diet preparation people.
6. Instrumentation calibration people.

These issues are discussed, however, in the "Personnel Plan Report," TR-477-23.

CAPACITY OF TOXICOLOGY TESTS PER MODULE

A special project was initiated to establish the annual testing capacity based upon incorporating one of each of the 63 modules. Table 8 correlates the number of tests per year per module as a function of test number. To illustrate the rodent acute oral exposure area (Module No. 1) can have 773 general toxicology tests done per year.

CONTINUOUS DEVELOPMENT OF REQUIREMENTS

Effective utilization of the Facility's capability requires continuous identification and interfacing with potential and actual users. The majority of these will be users whose needs are not currently being met (e.g., by the MRDC).

A Toxicology Requirements Plan should be developed that will provide an ongoing dialog between the Facility personnel and those of the Army's materiel developer (DARCOM).

ADAPTION TO CHANGING REQUIREMENTS

A project was completed to develop and recommend procedures whereby the Facility Manager would be able to adapt to changing Army mammalian toxicology requirements. Although the scope of the project is beyond the intent of this report, the recommendations identified are noteworthy. They are:

1. Plan for one to three years in advance.

2. Obtain firm commitments from those that will purchase the services so the money for overhead/people is available.

3. Avoid growing too rapidly especially without firm, funded user requests for service.

4. Maintain a constant awareness of the toxicology technology. This can most readily be accomplished by liaison with personnel of or Interagency Agreement with the NTP. The MRDC has, in fact, initiated steps towards such an agreement.

5. Utilize outside contracting firms as topping forces for overloads on equipment and facilities and service contracts for overloads on personnel.

TABLE 8 TESTING CAPACITY SUMMARY

Test No.	Title	Test Duration, D[a]	Module No.	Simultaneous No. of Tests in Module	Module Capacity Tests/Yr.[b]
1	Acute Oral Toxicity Study, Rodent	17	1	36	773
2	Subchronic Oral Tox. Study, Rodent	92	2	4	16
3	Chronic Oral Tox. Study, Rodent	817	3	2	1
4	Acute Inhalation Tox. Study, Rodent	25	5	6	142
5	Subchronic Inhalation Tox. Study, Rodent	100	6	3	11
6	Chronic Inhalation Tox. Study, Rodent	825	7	1	0.4
7	Acute Inhalation Toxicity Study, Primate	25	8	1	24
8	Subchronic Inhalation Tox. Study, Primate	100	9	2	7
9	Chronic Inhalation Toxicity Study, Primate	825	10	1	0.4
10	Subchronic Oral Toxicity Study, Dog	182	4	2	4
11	Acute Dermal Toxicity Study, Rabbit	16	11	7	160
12	Subchronic Dermal Toxicity Study, Rabbit	105	11	8	28
13	Acute Ocular Toxicity Study, Rabbit	14	12	14	365
14	Acute Delayed Neurotoxicity Study, Chicken	24	61	6	91
15	Subchronic Neurotoxicity Study, Chicken	92	61	6	24
16	Acute Dermal Irritation Study, Rabbit	5	11	58	4,234
17	Subchronic Dermal Irritation Study, Rabbit	22	11	8	133
18	Primary Eye Irritation Study, Rabbit	14	12	78	2,033
19	Dermal Sensitization Study, Guinea Pig	39	58	180	1,685
	Special Scientific Toxicology Studies				
S3a	Oncogenic Effects Oral Study, Rodent	902	16[c]	4	2
S3b	Reproductive Effects Study, Rodent	412	18	1	1
S3c	Teratogenic Effects Study, Rodent	37	19	3	30

-continued-

(a) Includes preparation and cleanup time.
(b) Rounded to nearest whole number if greater than or nearly equal to 1.0.
(c) Module 16 represents three different oncogenic study areas: rodent oral, rodent inhalation and primate inhalation.

Table 8 - continued

Test No.	Title	Test Duration, D[a]	Module No.	Simultaneous No. of Tests in Module	Module Capacity Tests/Yr.[b]
S3d	Combined Chronic Tox. & Oncogenic Effects Oral Study, Rodent	902	16[c]	2	1
S3e	Combined Reproduction/Teratogenic Effects Study, Rodent	412	18 or 19	1	1
S5	Subchronic Behavioral Effects Inhalation Study, Rodent	100	13[d]	1	4
S6a	Oncogenic Effects Inhalation Study, Rodent	902	16[c]	1	0.4
S6b	Combined Chronic Tox. & Oncogenic Effects Inhaltion Study, Rodent	902	16[c]	1	0.4
S8	Subchronic Behavavioral Effects Inhalation Study, Primate	100	13[d]	1	4
S9a	Oncogenic Effects Inhalation Study, Primate	902	16[c]	1	0.4
S9b	Combined Chronic Tox. & Oncogenic Effects Inhalation Study, Primate	902	16[c]	1	0.4
S20	In Vitro Genetic Toxicity Tests	31	62	3	35
S21	In Vivo Genetic Toxicity Tests	100	63	1	4

(a) Includes preparation and cleanup time.
(b) Rounded to nearest whole number if greater than or nearly equal to 1.0.
(c) Module 16 represents three different oncogenic study areas: rodent oral, rodent inhalation and primate inhalation.
(d) Module contains two testing areas, one for primates (large animals) and one for rodents (other small animals). Capacity based on testing in specified portion of module

TABLE 9 UNIQUE PLAN ELEMENTS - A TSCA PERSPECTIVE[a]

Function or Element	Planning Aspects	Principal Functions Involved	Problems	Opportunities
R&D	1. Review all existing projects 2. Include TSCA considerations in all future projects 3. Establish required liaison 4. Monitor projects based on TSCA developments 5. Plan for timing (PMN, PPN, etc.) requirements	R&D Requirements Finance Production & Engineering TSCA Manager/Coordinator	Increased cost Longer lead times Integration Complexities Limitations Increased personnel requirements Increased risk (failure, cost, investment, Sec 8(e) issues)	Product substitution Process substitution Component substitution Joint ventures Yield improvements
Testing	1. Establishment of testing programs a) Health b) Environmental } Outside c) Safety } Program d) Functional } Scope 2. Cost determinations 3. Lead Times 4. Integration with other needs 5. Budgeting 6 Monitoring for current protocols	R&D Safety & Health Government relations TSCA Manager/Coordinator Requirements	Uncertainties Costs Lead times Potential 8(e) issues Increased R&D lead times Higher risk	Basic research in toxicology Reduced potential product hazards
Lead Times	1. Review of existing projects and programs 2. Inclusion in future projects and programs of revised time tables based on TSCA 3. Integration with other activities	R&D Manufacturing & Engineering Requirements	Uncertainties Temporal increases Cost of time increases Fielding delays Increased investment risk	None visualized
Production and Engineering	1. Review of present projects and programs 2. Inclusion in future projects and programs 3. Timing factors 4. Risk factors 5. Quality control elements 6. Monitoring for TSCA developments as they may alter projects 7. Consideration of process and pilot plant production 8. Synchronization with other activities	Manufacturing Engineering Government relations TSCA Manager/Coordinator Requirements Logistics	Increased complexity Increased cost Higher Risk Longer lead times	Process development Yield improvements Reduction in impurities, by-products, etc. Development of less hazardous processes Cost reductions (if they can be found)
Cost Sharing	1. Consideration under TSCA Sec. 4 & 5 2. Joint efforts through DOD 3. Business ventures with suppliers 4 Joint efforts between manufacturers and users	Management Requirements Legal Finance	Sharing of testing or development costs Requirements Limitation Legal risks	Joint ventures New supplier/user relationships Spreading of financial risk Improved investment certainty

a. The intention of this table is not to be all-inclusive but rather to provide some insights into the range of possible practical considerations that should be incorporated in TSCA plans. The experience of individual Army organizations and their needs will, undoubtedly, enable the addition of numerous other factors within each element tabulated as well as the addition of other plan elements.

6. Devote the limited resources available to the establishment of protocols and capabilities for Army-unique toxicology research/testing requirements. These are the most difficult to acquire on the outside.

Plan Elements

Table 9 presents a modification of a plan to meet one, of many regulatory requirements being imposed on the Army -- TSCA (Dominguez, 1979, p. 238). This plan could be expanded to include other regulatory and nonregulatory requirements. It is presented to show a method, no a final answer. The Plan looks at the R&D function, testing function, lead time functions, production and engineering functions and cost sharing.

CONCLUSIONS

A toxicology facility to handle all of the project Army requirements does not exist. Addition of new capability and capacity is recommended. These parameters are a function of MRDC/DA decision-making processes. A modular design was conceived to provide for a full-service capability. This permits the decision-makers the option to readily pick and choose from options presented which capabilities and capacities are desired based upon requirements, priorities, budgets, personnel resources, etc.

The Facility must provide for scientifically sound technical results, able to be scrutinized by peer groups, regulatory agencies and standard and criteria developers.

RECOMMENDATIONS

The following recommendations are made:

1. Divide the facility into two major capabilities, initial and growth.

2. Use a step-wise increase in capability within each of the two stages to effectively integrate capability and personnel with available resources and ability to simulate the growth.

3. Because toxicology is very much a science oriented discipline and the results are dependent upon scientists, the manner in which the work is carried out and the standards should be controlled directly by a Facility Science Director in conjunction with an all Army review team, a non-Army review team and a peer group of advisors.

4. The specific tests utilizing standard protocols, the new protocols to be developed, the special scientific experiments to be carried out and the genetic toxicology tests to be included must all be finalized prior to initiation of a Facility development Plan.

5. One of several companies noted for their techniques in scheduling toxicology testing activities should be contacted to obtain proven procedures for minimizing overloads of facilities and equipment and excessive workloads on personnel in short supply.

6. A decision must be made to determine which of the following animals should be included within the Facility's capability, rodents (mice, rats, guinea pigs), primates, rabbits, dogs and chickens (the latter used only for neurotoxicology).

7. Special emphasis should be made to incorporate a training function to provide the Army with personnel for:

   a. Determining toxicology requirements as a function of materiel development cycle.

   b. Inspectors to be utilized to ensure standards and criteria are being met.

   c. Develop personnel to relieve those known to be in limited supply (e.g., veterinarian pathologist) and to train a generation of middle and lower level technical supporting personnel.

REFERENCES

Dominguez, GS. 1979. The business guide to TOSCA, effects actions. New York, NY: John Wiley and Sons, pp. 116, 120, 238.

ICF, Inc. 1980. Profile of the chemical safety testing industry: an assessment of pesticide testing capacity. Final report. Washington, DC: ICF, Inc. U.S. Environmental Protection Agency.

Development Planning and Research Associates, Inc. and ICF, Inc. 1980. Chemical testing industry study. Work plan report. Washington, DC: Development Planning and Research Associates, Inc. U.S. Environmental Protection Agency contract no. 68-01-6064.

APPENDIX I PUBLIC LAWS THAT REQUIRE TOXICOLOGY TESTING AND AFFECT TOXICOLOGY RESEARCH FACILITIES

Department	Agency/ Administration	Public Law Title	Acronym	Public Law and Amendments Number	Public Law and Amendments Date	Material or Scope of Work	Tox. Testing Direct	Tox. Testing Indirect	Facility Compliance Requirements Direct	Facility Compliance Requirements Indirect
—	EPA	Federal Insecticide, Fungicide, Rodenticide Act	FIFRA	92-516 94-140 95-396	10/21/72 11/28/75 9/30/78	Pesticides	X	—	X	—
—	EPA	Toxic Substances Control Act	TSCA	94-469	10/11/76	Hazardous and Toxic Substances	X	—	X	—
—	EPA	Resource Conservation and Recovery Act	RCRA	94-580 95-609 96-482	10/21/76 12/8/78 12/8/78	All Hazardous Materials	—	X	X	—
—	EPA	National Environmental Policy Act	NEPA	91-190 94-83	1/1/70 8/9/75	All Fed. Gov't. Activities	—	X	—	X
—	EPA	Clean Water Act	CWA	92-500 95-217 95-576 96-483	12/27/77 11/2/78 11/2/78 11/2/78	Pesticides, Metals and Organics	—	—	—	X
—	EPA	Safe Drinking Water Act	SDWA	93-573 95-190 96-63 96-502	12/16/74 12/8/78 12/8/78 12/8/78	Pesticides, Metals and Organics	—	—	—	X
—	EPA	Clean Air Act	CAA	91-604 95-95	8/7/77	Particulates and Other Pollutants	—	—	—	X
DOL	OSHA	Occupational Safety and Health Act	OSHA	91-596	12/29/70	Workplace Hazards	—	X	X	—
USDA	—	Animal Welfare Act	AWA	89-544 91-579 94-279	8/24/66 12/24/70 4/22/76	Animals	—	—	X	—
DHHS[a]	FDA	Federal Food, Drug and Cosmetic Act	FFDC	52-1040	6/25/38	Foods, Drugs and Cosmetics	X	—	X	—
DHHS	FDA	Public Health Service Act	PHSA	58-682	7/1/44	Biological Products	—	X	—	X
—	CPSC	Consumer Product Safety Act	CPSA	92-573 94-284 95-319 95-631	10/27/72 5/11/76 7/11/78	Consumer Products	X	—	—	—
—	CPSC	Federal Hazardous Substances Act	FHSA	86-613 95-631	7/12/60 11/10/78	Consumer Products	—	X	—	X
DOT	MTB	Hazardous Materials Transportation Act	HMTA	93-633	1/3/75	Explosives, Pesticides and Organics	X	—	X	—
DOE	NRC	Atomic Energy Act	AEA	83-703	8/30/54	Radioactive Compounds	—	—	X	—

(a) Department of Health and Human Services, formerly Department of Health, Education and Welfare

APPENDIX 2

PERSONNEL AND FACILITY ACCREDITATIONS AND CERTIFICATIONS

Personnel Certification

1. American College of Veterinary Medicine for Veterinary Pathologists
2. ASCP for Histology Technicians and Chemical Chemistry Technicians
3. American Association of Laboratory Animal Sciences for Animal Technicians and Caretakers
4. American Board of Toxicology
5. American College of Veterinary Pathologists (ACAP)
6. American College of Laboratory Animal Medicine (ACLAM)
7. American Board of Veterinary Toxicology
8. American Board of Clinical Chemistry
9. National Registry in Clinical Chemistry
10. American Society of Clinical Pathology

Facility Accreditations

1. Good Laboratory Practices, FDA
2. Good Laboratory Practices, EPA
3. American Association for Accreditation of Laboratory Animal Care
4. U.S. Department of Agriculture
5. Toxicology Laboratory Accreditation Board
6. Toxicology Laboratory Animal Board

APPENDIX 3 TYPICAL ONGOING TASKS PROVIDED BY A FULL-SERVICE FACILITY

Before Testing

1. Monitor and maintain knowledge of toxicology testing capabilities available to fulfill medical and non-medical military needs
2. Perform continuing analysis of military user (e.g., DARCOM) needs for toxicology testing
3. Identification of waste products from munitions, synthetic fuels, etc.
4. Determine and maintain priority setting mechanisms to select the most important chemicals for tests
5. Prepare and maintain long range R&D Plan (per AR 70-55 (paragraph 9b) and AR 70-1 (paragraph 1-8b))
6. Service as expertise and appropriate data base to evaluate specific toxicology research testing requirements for the MRDC on a continuing basis (movie versus snapshot)
7. Review health records on exposed populations. This would include morbidity and mortality reports
8. Perform measurements on suspected exposed population and compare with control group. This could include both prospective and retrospective studies
9. Identify potentially toxic materials (chemicals)
10. Provide Advice/Recommendations on Toxicology Testing Needs
11. Literature and Information Reviews/Searches (To Minimize Toxicology Testing Needs)
12. Basic Research on Toxicology Testing (to develop techniques to extrapolate more effectively from animal data to humans)
13. Hazard assessment scientific data base to support a cost-effective procedure for evaluating the environmental hazard of Army wastes and for complying with waste treatment and disposal requirements
14. Improved methods for evaluating animal test data and making species extrapolations to humans for predicting toxic substance effects on troops under military training/combat conditions
15. Sensitive and cost effective test procedures for evaluation of organ toxicity for use in testing
16. Short-term *in vivo* test predictive of oncogenic potential of chemicals and chemical mixtures for use in assessing military toxic hazards within time and cost constraints

17. Sensitive and relevant behavioral tests for prediction of human performance decrement from toxic substance exposure of troops under training/combat conditions

18. Improved toxicologic test procedures for predicting toxic substance effects on troops exposed under realistic field training/combat conditions

19. Improved sensitive test systems for evaluating and predicting the interactive effects of toxic substances and other stresses on troops under realistic field exposure conditions

20. Short-term test procedures for evaluating Army relevant environmental pollutants with reduced time and cost requirements

21. Chemically and physically characterize potentially toxic materials - so it can be simulated in the laboratory to obtain the toxicology data

During Testing

22. Toxicology Testing (Limited Scope)

23. Toxicology Testing (Medium Scope)

24. Toxicology Testing (Full Scope)

In Parallel with Testing

25. Develop toxicology (health effects or hazard assessment) data-base (toxicologic and/or epidemiologic studies)

26. Quality Assurance Services

27. Regulatory Affairs

28. Provides Training of Army Personnel

After Testing

29. Establish criteria to avoid reversible toxic effects

30. Establish criteria to avoid irreversible toxic effects

31. Sensitive and cost-effective procedures for evaluating Army relevant environmental pollutants to base environmental quality protection criteria

APPENDIX 4 SERVICES THAT COULD BE PROVIDED FOR EACH ASSIGNMENT

1. Review materiel/equipment test plans and design concepts
2. Evaluate range of scenarios for exposure to toxic materials (a chemical or mixture of chemicals)
3. Alert DA to requirements
4. Alert DA to areas of vulnerability
5. Recommend course(s) of action
6. Respond to requests to do work
   a. Get facts, report back
   b. Expand involvement
7. Take action needed
8. Indicate toxicologic data inputs required
9. Literature review on health effects of exposures (including, where applicable, all material projected for use in the manufacturing process to determine work completed by others)
10. Problem Definition Study
11. Evaluation of literature on health effects for given type(s) of exposures
12. Applicability of existing protocols to military unique exposures
13. Production Process Evaluation Study - Specific chemicals, exposures
14. Risk Assessment Analysis (Health/Environmental)
15. Health Hazard Assessment Analysis
16. Recommend concepts for protection against hazard(s)
17. Recommend materials for protection against hazard(s)
18. Identification of Specific Testing Requirements
19. Identification of Specific Research Requirements
20. Select Methodology, have Peer Review
21. Establish applicability of animal models to military unique exposures to hazard requirement. Determine best animal models for various chemical tests (this could be considered part of the protocol preparation)

22. Carry out epidemiology Studies

23. Decide if to test or not and priority

24. Chemically (analytically) characterize potentially toxic materials or environments -- so it can be simulated in the laboratory to obtain the toxicology data. Chemistry literature review to:

    a. Determine anticipated products
    b. Develop capability to characterize (sampling, analytical approaches, etc.)

        1. Laboratory
        2. Field

    c. Do analysis
    d. Determine how to duplicate for mammalian toxicology testing

25. Physical (chemical) aspects of:

    - Physical form (gas, liquid, solid)
    - Chemical specie (e.g., valence state of metal)
    - Route(s) of exposure
    - Magnitude of concentration peak
    - Duration of exposure
    - Frequency of exposure
    - Intervals between exposures

26. Physically characterize the form of chemicals, e.g., particle size and distribution of a smoke

27. Develop chemical generation simulators to allow reproduction of chemical and physical characteristics in the toxicology laboratory

28. Develop exposure equipment that will enable the tests to duplicate the exposure levels, duration and multiple stresses

29. Actual Industrial Environment Characterization

30. Characterization of Soldier's Field Operating Environments

31. Make in-plant and in-field measurements over time with variations in raw material, production, processes that produce the material, standard levels of maintenance of equipment, operation under different climatic conditions such as temperature, humidity which may impact by-product formation rate or actual formation

32. Identification of new toxicity tests/protocols needed

33. Develop methodology and indicate data inputs required

34. Decision on route(s) of exposure

35. Clinical Studies

36. Establish Test Methodology (Preparation of protocols and analytical chemical procedures prior to "production type" research/testing.)

37. Weigh the importance of data inputs

38. Synthesis chemicals

39. Validate new toxicity tests/protocols

40. Measure toxicology through proper conduct of required studies

41. Complete selected Toxicology Evaluation Studies (General ..... Behavioral)

42. Establish standardized new toxicity tests/protocols

43. Complete comparative metabolism studies.

44. Establish dose-response relationship for all identified end points

45. Apply safety factors

46. Complete inter- and intra-species extrapolation and low to high concentration levels extrapolation

47. Identify and recommend protection required

48. Provide guidance for The Surgeon General and TRADOC users

49. Identification of interaction mechanisms

50. Establish environmental quality protection criteria recommendations

51. Recommend criteria

52. Establish criteria to avoid reversible toxic effects

53. Establish criteria to avoid irreversible toxic effects

54. Recommend occupational health protection criteria

55. Recommend occupational health exposure limits

56. Transfer technology to literature, other users, etc.

57. Recommend surveillance techniques

58. Recommend treatment procedures

59. Identify modifications of soldier capabilities in using

60. Expand Health Hazard Assessment Data Base

61. Complete retrospective epidemiology

62. Complete re-evaluation of standards

APPENDIX 5

ROUTES OF EXPOSURE AND ADMINISTRATION

Cutaneous
Dermal
Epidural
Eye instillation
Immersion
Implantation, Surgical
Inhalation
  Vapor
  Aerosol
  Particulate
Interdermal
Intracardiac
Intracoelomic and muscular
Intracutaneous
Intradermal
Intradiscal
Intragastric
Intrahepatic
Intralaryngeal
Intralingual vein
Intramuscular injection
Intraocular
Intraperitoneal (i.p.)
Intrapleural
Intrarectal
Intrarenal
Intrasalivary gland
Intrathoracic
Intratracheal
Intratympanic (middle ear)
Intrauterine (i.u.)
Intravaginal
Intravenous injection (i.v.)
Intravesicular
Introdermal injection
Inunction
Ocular
Oral
  Food/Diet
  Gastric Intubation
  Gavage
  Capsule
  Peros
Parenteral
Percutaneous
Rectal
Skin painting
Subcutaneous (s.c.) injection
Suppository
Topical
Vitreal injection

APPENDIX 6

FACILITY AREAS/LABORATORIES

Areas of Major Importance

1. Acute Oral Exposure Area, Rodent
2. Subchronic Oral Exposure Area, Rodent
3. Chronic Oral Exposure Area, Rodent
4. Subchronic Oral Exposure Area, Dog
5. Acute Inhalation Exposure Area, Rodent
6. Subchronic Inhalation Exposure Area, Rodent
7. Chronic Inhalation Exposure Area, Rodent
8. Acute Inhalation Exposure Area, Primate
9. Subchronic Inhalation Exposure Area, Primate
10. Chronic Inhalation Exposure Area, Primate
11. Dermal Testing Area, Rabbit
12. Ocular Testing Area, Rabbit
58. Dermal Testing Area, Rodent
13. Behavioral Studies Area
14. Metabolism/Pharmacokinetics Studies Area
15. Pharmacodynamics Studies Area
16. Oncogenic Studies Area
17. Respiratory Physiology Studies Area
18. Reproduction Studies Area
19. Teratology Studies Area
61. Neurotoxicology Studies Area, Chicken
62. In Vitro Genetic Toxicology Studies Area
63. In Vivo Genetic Toxicology Studies Area

Areas of Intermediate Importance

20. Food Preparation/Blending Area
21. Non-radioactive Waste Handling/Disposal Area
22. Refrigerated Food Storage Area
23. Quality Assurance Laboratory
24. Animal Quarantine Area
25. Pathology Laboratory
26. Clinical Chemistry Laboratory
27. Animal Breeding Area
28. Veterinary Medicine Area
29. Analytical/Synthetic Chemistry Laboratory
30. Automated Data Processing Area
31. Radiochemistry Laboratory

Areas of Minor Importance

32. Cage/Rack Washing and Storage Area
33. Chemical Storage Area
34. Showers, Lockers and Toilets Area
35. Glassware Washing Area
36. Library Area
37. Technical Offices Area

continued -

60. Administrative Office Area
38. Shipping and Receiving Area
39. Luncheon Room Area
40. Record Archives Area
41. Specimen Storage Area
42. Linen Storage Area
43. Janitorial Storage Area
45. Equipment Maintenance Area
46. Laundry Area

Facility Central Utilities Areas

44. Central Cylinder Gas Storage Area
47. Central Power Area
48. Central Standby (Emergency) Power Area
49. Central Water Supply Conditioning Area
50. Central Wastewater Conditioning Area
51. Central Air Handling Area
52. Central Heating Area
53. Central Compressed Air/Vacuum Area
54. Central Communications Area
55. Central Refrigeration Area
56. Central Toilet Area
57. Central Vacuum Cleaning Area
59. Central Automated Facility Systems Control Area

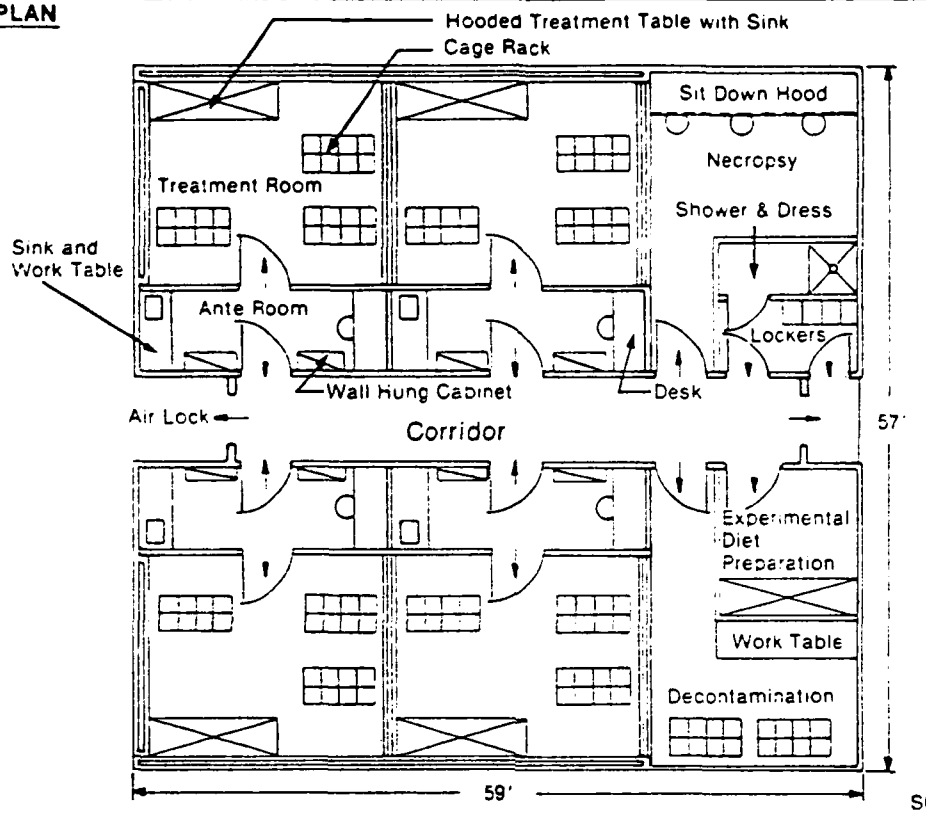
APPENDIX 7

EXAMPLES OF FACILITY CAPABILITY MODULES

MAMMALIAN TOXICOLOGY FACILITY MODULE DESCRIPTION

Life Systems

FLOOR PLAN



CONSTRUCTION INFORMATION

Dimensions: 59 x 57 Ft.
Area: 3,363 Sq. Ft.
Ceiling Height ☐ 8' ☒ 9' ☐ 13' ☐ _____
Air Flow: 7,500 CFM ☐ Variable
Air Changes/Hour: 15
Floor Drains: ☒ Capped ☐ Flushing ☐ Other
Water: ☒ Hot ☒ Cold ☐ None ☐ No ☐ Make-up
Central Vacuum Cleaning: ☒ Yes ☐ No
Local Exhaust Filtration: ☒ Yes ☐ No
Epoxy Coated: ☒ Walls ☒ Floors ☒ Ceilings
Sprinklers: ☐ Yes ☒ No ☐ Halon ☐ Optional
☒ Timed Lighting
☐ Compressed Air; ☐ Vacuum; ☐ Other Gases
☐ Emergency Shower/Eye Wash

SPECIAL FEATURES/BENEFITS

1. Can test four chemicals simultaneously.
2. Double walls for air pressure control in rooms and sound isolation.
3. Compatible with highly hazardous tests:
   - Ante room isolates corridor
   - Local diet preparation
   - Local necropsy
   - Local cage/rack decontamination

SPECIAL ASSUMPTIONS

1. Tests of highly hazardous materials must be performed.
2. Safety considerations require local necropsy and diet preparation.

COST ESTIMATE

	Total $(000)	Resulting $/Sq. Ft.
General Construction	54	16
Heat, Vent., Air Cond.	34	10
Electrical	31	9
Sanitary	16	5
Equipment	104	31
Total	239	71

TITLE Acute Oral Exposure Area, Rodent

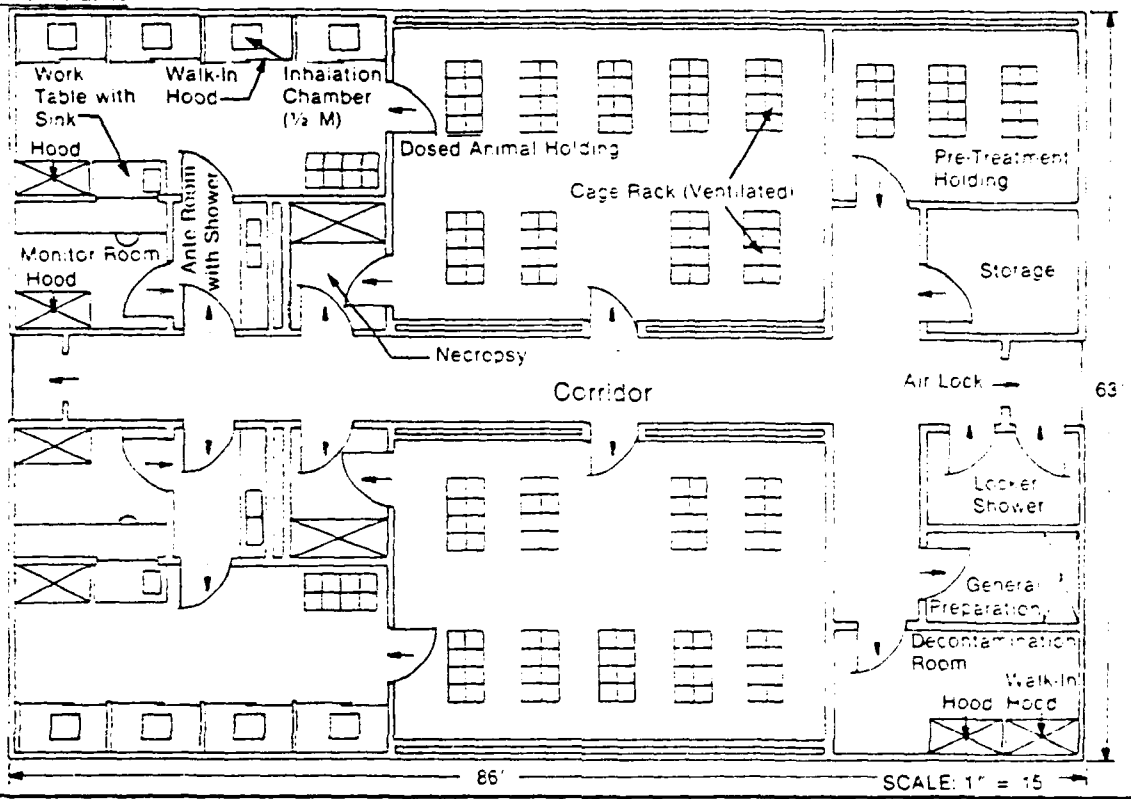
NO. 1

F-650 (2/15/81)

MAMMALIAN TOXICOLOGY FACILITY MODULE DESCRIPTION

Life Systems

FLOOR PLAN



CONSTRUCTION INFORMATION

Dimensions: 86 x 63 Ft.
Area: 5,418 Sq. Ft.
Ceiling Height ☐ 8' ☒ 9' ☐ 13' ☐ _____
Air Flow: 12,000 CFM ☐ Variable
Air Changes/Hour: 15
Floor Drains: ☒ Capped ☐ Flushing ☐ Other
Water: ☒ Hot ☒ Cold ☐ None ☐ No ☐ Make-up
Central Vacuum Cleaning: ☒ Yes ☐ No
Local Exhaust Filtration: ☒ Yes ☐ No
Epoxy Coated: ☒ Walls ☒ Floors ☒ Ceilings
Sprinklers: ☐ Yes ☒ No ☐ Halon ☐ Optional
☒ Timed Lighting
☐ Compressed Air; ☐ Vacuum; ☐ Other Gases
☐ Emergency Shower/Eye Wash

SPECIAL FEATURES/BENEFITS

1. Can test two chemicals simultaneously.
2. Separate dosed animal holding areas avoids cross-contamination.
3. Walk-in hoods provide safe maintenance of chambers from all sides.
4. Compatible with highly hazardous tests:
   - Ante room permits personnel decontamination
   - Local necropsy
   - Local decontamination

SPECIAL ASSUMPTIONS

1. Desirable to have local pre-test animal holding area.
2. Desirable to have local necropsy.

COST ESTIMATE

	Total $(000)	Resulting $/Sq. Ft.
General Construction	124	23
Heat Vent., Air Cond.	74	14
Electrical	71	13
Sanitary	38	7
Equipment	398	73
Total	705	130

TITLE
Acute Inhalation Exposure Area, Rodent

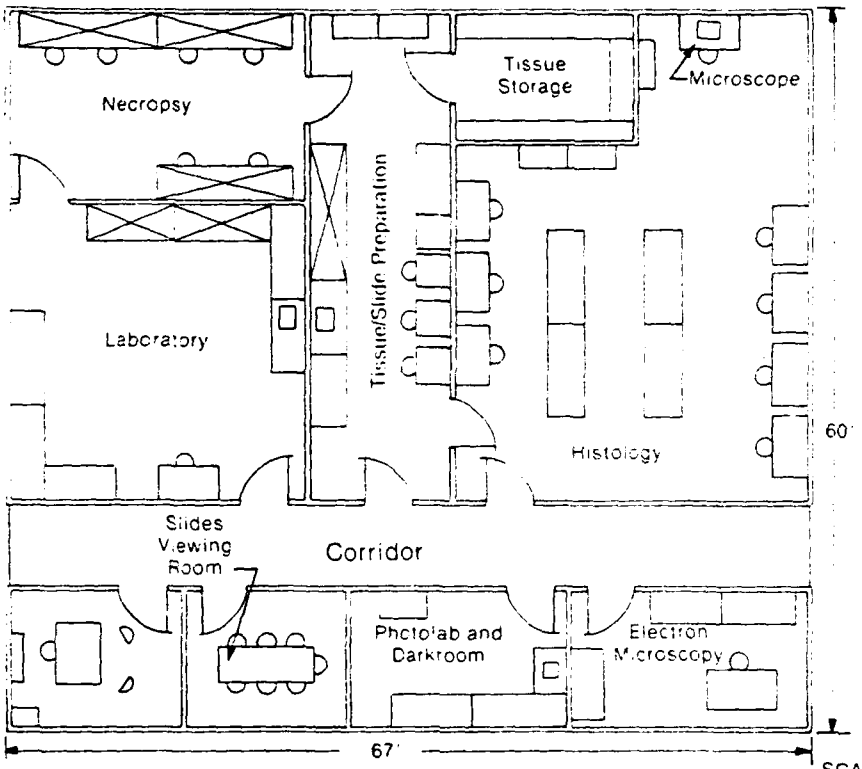
NO. 5

F-650 (2/15/81)

MAMMALIAN TOXICOLOGY FACILITY MODULE DESCRIPTION

Life Systems

FLOOR PLAN



SCALE: 1" = 15'

CONSTRUCTION INFORMATION

Dimensions: 67 x 60 Ft.
Area: 4,020 Sq. Ft.
Ceiling Height ☐ 8' ☒ 9' ☐ 13' ☐ _____
Air Flow: 9,000 CFM ☐ Variable
Air Changes/Hour: 15
Floor Drains: ☐ Capped ☐ Flushing ☒ Other
Water: ☒ Hot ☒ Cold ☐ None ☐ No ☐ Make-up
Central Vacuum Cleaning: ☐ Yes ☒ No
Local Exhaust Filtration: ☐ Yes ☒ No
Epoxy Coated: ☒ Walls ☒ Floors ☒ Ceilings
Sprinklers: ☐ Yes ☒ No ☐ Halon ☐ Optional
☐ Timed Lighting
☒ Compressed Air: ☒ Vacuum: ☒ Other Gases
☒ Emergency Shower/Eye Wash

SPECIAL FEATURES/BENEFITS

1. Laboratory sized for sacrificing large primates.
2. Capability for histopathology investigations with light or electron microscopy.
3. Capability for group viewing of slides.

SPECIAL ASSUMPTIONS

None.

COST ESTIMATE

	Total $(000)	Resulting $/Sq. Ft.
General Construction	48	12
Heat. Vent. Air Cond	36	9
Electrical	36	9
Sanitary	24	6
Equipment	445	111
Total	589	147

TITLE Pathology Laboratory

NO. 25

F-650 (2/15/81)

APPENDIX 8

ALPHABETICAL INDEX OF BUSINESS SERVICES

continued -

Appendix 8 - continued

Contract Personnel (File)
Contract Program Billing
Contracting, Electrical
Contracting, General
Contracting, Mechanical (AVAC)
Contracting, Plumbing
Control/Monitor Instrumentation
Controlled Substances
Controller, Corporate
Cost Control
Cost-of-Living (Calculation of)
Cost-to-Complete
Customer Contact Report
Customer Liaison

Data Communications
Data Processing
Data Reduction
DCAA Interface
Deferred Compensation
Design/Drafting
Documentation (See Word Processing Center)
Drafting (See Design/Drafting)
Duplication

Electronic Software Management
Employment Recruiting, Permanent
Employment Recruiting, Temporary
Engineering Laboratory
Engineering Technology
Equal Employment Opportunity
Equipment Servicing and Maintenance
Expendables (See Purchasing)
Expense Account Control System
Experimental Design

Fabrication Kit (See Purchasing)
Facility
Facility Layout
Facility Resources
Facility Servicing and Maintenance
Facility Utilities[a]
Field Service
Final Report
Final Report Coordination

(a) Electricity, heat, air conditioning, backup power, sanitary, etc.

continued -

Appendix 8 - continued

Financial Report
Fire Alarms
Fire Extinguisher
First Aid
Fiscal Year Record
Fixtures (See Jigs, Fixtures & Molds Control System)
Food Preparation/Blending
Forms Control
Forms Revisions and Updating

Gases (See Compressed Gases)
Gauge Calibration System
Glass Washing
Government Property Control

Hazardous Material Disposal
Hazardous Material Handling
Heating (See Facility Utilities)

Indoctrination
Inspection
Instrumentation (See Equipment)
Instrumentation Laboratory
Insurance
Invoicing (See Bookkeeping)

Janitorial Service
Jigs, Fixtures & Molds Control System

Key Control System
Keypunch Control System

Label
Laboratories (See individual ones)
Laboratory Animals (See Animals)
Laundry
Law Suits
Lease Agreement Preparation
Letters, Filing Yellow Copy
Library/Librarian
Literature Review
Local Pickup and Delivery (See Pickup and Delivery)
Log Book Control
Long-Lead Item Procurement
Lunchroom

continued -

Appendix 8 - continued

Machine Shop
Mail Service/Room
Maintainability Technology (See Product Assurance)
Maintenance
Maintenance Agreement
Management Planning Procedure
Mask (See Expendables)
Material Control (See Material Services)
Material Services
Mathematical Model Technology
Mechanical Engineering Technology
Microbiology Technology
Mockup
Mold (See Jigs, Fixtures & Molds Control System)
Monthly Trial Balance (See Accounting)
Moves (Facility, Equipment)

New Technology
Notebooks, Laboratory
Notes (See Word Processing Center)

Office Supplies
Offices
Operating Procedures File
Outside Services
Overtime

Packaging
Parts Stores
Pathology Laboratory
Patents
Payroll Computing and Preparation
People Power Log
Performance (Quality) Control
Personnel
Petty Cash
Photograph/Presentation File
Photography
Phototype Setting
Pickup and Delivery, Local
Pollution Laws/Regulations
Postage
Precious Metals
Presentation Preparation
Presentations File
Printing Service
Procedures

continued -

Appendix 8 - continued

Procurement Regulations
Product Assurance
Program Management
Program Managers
Project Assignment File
Project Assignments
Property Accountability
Proposals
Protocols
Purchasing

Quality Assurance (See Product Assurance)
Quality Control (See Product Assurance)

Radiochemistry (Labeling, Counting)
Rate Justification
Receipt of Award Log
Receiving
Reception
Recruitment
Refrigerated Food Storage
Refuse Pickup/Disposal
Reliability
Rentals (See Purchasing)
Repairs
Repairs (Unscheduled Maintenance)
Research
Rest Rooms
Review Meetings

Safety
Sanitary (See Facility Utilities)
Schedule Control
Science
Secretarial Services
Security/Access Control
Sensors, Analyzers and Monitors (SAM)
Shipping (Including Packaging and Transportation)
Shutdown Procedure
Soda Pop Service
Software
Special Studies
Specimen Storage
Standard Operating Procedures (SOPs)
Startup Procedure
Statistics

continued -

Appendix 8 - continued

Storage
Stores
Suits
Supplemental Unemployment Benefit (SUB)
Supplier Review Meeting
Supplier Source Inspection
Systems Engineering Technology

Taxes
Technical Papers
Technician Coordination/Administration
Technology
Telegram/Night Letter Service
Telephone Service
Terminations
Test Support Accessories (TSA)
Testing Underway
Thought Tank
Time Cards
Tools and Tool Boxes
Training Program
Transportation
Travel Advance
Travel and Business Expense
Travel Arrangements

Varityper Operation
Vehicle Use Log
Ventilation (See Facility Utilities)
Veterinary Medicine
Vice President's Office
Viewgraph Preparation, Files, Supplies
Viewgraphs
Visas

Warehouse (See Storage)
Washing (Glassware, Laboratory Apparatus)
Washrooms
Welding
Word Processing Center
Work Schedule

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USAMRDC (SGRD-RMS)
Fort Detrick
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Cameron Station
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