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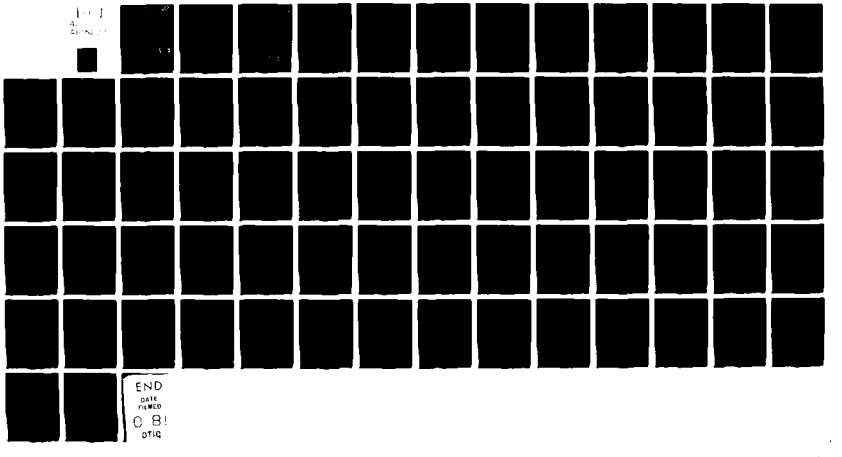

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EVALUATION OF SHORT-TERM BIOASSAYS TO PREDICT FUNCTIONAL IMPAIRMENT

Development of Cardiovascular Bioassays in Laboratory Animals
Directory of Institutions/Individuals
Final Report

Richard Thomas
Purna Greenaway

October 1980

Supported by

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

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The MITRE Corporation
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McLean, Virginia 22102

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US ARMY MEDICAL BIOENGINEERING RESEARCH AND DEVELOPMENT LABORATORY
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Cardiovascular toxicity	Functional monitoring	Test systems utilized
Directory	Morphological alterations	
Research organizations	Biochemical measurements	Compounds tested
Perfused heart preparations	Cultured heart cells	Toxic substances

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

MITRE has been requested by the U.S. Army Medical Bioengineering Research and Development Laboratory to identify and evaluate short-term bioassays which have demonstrated ability to evaluate and predict cardiovascular impairment resulting from toxicant exposures. This directory is a companion to Selected Short-Term Cardiovascular Toxicity Tests, DAMD 17-78-C-8068, which describes the available cardiovascular testing protocols and assesses their suitability for a program. This directory catalogues the organizations currently engaged in cardiovascular bioassay utilization or development and provides information

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

20. Abstract (Con't)

concerning specific measurements performed, test systems employed, compounds tested, requirements for anesthesia and terminal nature of the test.

In the companion report, MITRE reviewed and recommended short-term tests for evaluating and predicting the functional and/or morphological impairment produced by toxic substances using animal test systems. The document presents information on the available tests for the cardiovascular system and recommends those tests which are suitable for use in a screening program.

A variety of testing techniques have been developed to detect cardiovascular damage; however, few of these are well developed or have demonstrated ability to detect damage in short-term screening. Those tests that are sufficiently developed to have potential application in a short-term screening program for cardiotoxicity are described in the report. The information in the report deals only with animal testing. The testing techniques used in humans are included only if they might prove useful in animal testing.

After an assessment of the cardiovascular testing techniques was made, none of the techniques sufficiently satisfied the criteria to be immediately useful in a short-term screening program. Nonetheless, a battery of tests are recommended that show the greatest potential utility in a cardiovascular screening program.

The recommended tests include both in vivo and in vitro techniques. The in vivo functional techniques recommended are the monitoring of left ventricular pressure, arterial pressure, aortic flow, cardiac output and electrocardiographic activity. The morphological techniques recommended include gross inspection, light microscopy and limited electron microscopy. The biochemical analyses recommended include serum lactic dehydrogenase (LDH), creatine phosphokinase (CPK) and tissue electrolytes (e.g., magnesium, calcium, sodium and potassium). The in vitro techniques recommended are cultured heart cells and perfused heart preparations. In both the cell cultures and perfused heart preparations, various biochemical (e.g., LDH, CPK) and functional (e.g., beating and electrical activity) parameters may be monitored.

Some experimental procedures currently in the research and development stage are briefly discussed for their future potential as screening tests.

EXECUTIVE SUMMARY

The MITRE Corporation, Metrek Division is currently assisting the United States Army Medical Bioengineering Research and Development Laboratory (USAMBRDL) in the development of a hierarchical short-term testing scheme to screen substances for functional or morphological impairment in animal test systems. Effects in four organ systems--pulmonary, hepatic, renal and cardiovascular--are being considered.

As part of this effort, Metrek has been asked to prepare directories of organizations and individuals presently involved in the development and/or utilization of tests applicable to toxicity screening. This directory serves as a companion document to the report, Evaluation of Short-Term Bioassays to Predict Functional Impairment: Selected Short-Term Cardiovascular Toxicity Tests.

Entries in this directory for several organizations currently involved in the organ bioassay use or development include at least one contact individual's name, which appears under the organization name and address at the top of the page. These are the people who, during the process of directory compilation, described either their activities or the activities of their group regarding organ toxicity testing, and thereby provided the information presented in the entry. The information provided includes the specific tests and observations performed; the test systems utilized (e.g., experimental animals or

tissues in vitro); the substances administered or conditions established to elicit toxic response (e.g., stress); the use of anesthesia, and the terminal nature of the tests conducted.

In order to facilitate use and the processes of amending and adding to the directory, it has been arranged in alphabetical order by organization. In order to further simplify use of the directory, three indexes have been prepared and are included as appendices. The first, Appendix A, is an alphabetical index of tests performed by each organization engaged in developing, performing or refining the tests noted. Appendix B is an alphabetical index of species utilized, and all the organizations employing each test system. These are further divided by tests performed. In this way it is possible to ascertain which organizations perform particular bioassays in a specific test system. Appendix C is an alphabetical index of the individuals mentioned in the directory, and the organization with which they were affiliated when contacted.

The objective of this directory is to provide a readily usable guide to that segment of the scientific community currently active in organ system toxicity testing in animals. Because research associate and graduate student positions are often temporary in nature, a deliberate attempt was made to exclude these individuals from the directory. Their efforts, however, are likely to be represented by activities associated with their organization, as in most cases these individuals are conducting research under the

auspices of someone more senior and more permanently allied with the organization, who was included in the directory. In addition, there are individuals who were active in toxicity testing at one time but are no longer; these have also been omitted from the directory. The efforts of many of those who are not currently active, but were involved over a period of many years and distinguished themselves in the field, are reflected in the report, Selected Short-Term Cardiovascular Toxicity Tests.

Some of the entries in the directory may be less detailed than others, and less specific in the detail that is presented. In addition, the information presented for an organization may not be reflective of all the ongoing efforts at that organization. This is due largely to the reluctance of some individuals contacted to communicate the information and, in small part, to an inability to contact a few individuals at the time this directory was being compiled. The information in the directory was selected to provide an immediate indication of the practices of each organization concerning some issues of importance when designing a screening program. Much of this information is discussed in greater detail in the report, Selected Short-Term Cardiovascular Toxicity Tests.

FOREWORD

This Directory was compiled by MITRE staff by means of a survey of the recent literature, and by discussions with leaders in the field and other personal contacts. We are grateful to all those who responded so patiently to our questions regarding their activities. All of the "contact persons" were given an opportunity to review the information relating to their organization. We recognize there may be inadvertent omissions for which we offer our sincere apologies.

Citations of organizations and tradenames in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

TABLE OF CONTENTS

DIRECTORY OF ORGANIZATIONS CURRENTLY INVOLVED IN UTILIZATION OR DEVELOPMENT OF CARDIOVASCULAR TESTS IN LABORATORY ANIMALS

ORGANIZATION:

ALLIED CHEMICAL
BOX 1021R
MORRISTOWN, NEW JERSEY
S.C. GAD (201) 455-6085

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS
CULTURED MYOCARDIAL CELLS
WHOLE ANIMAL FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

ANTIOXIDANT SUBSTANCES SUCH AS BUTYLATED HYDROXYTOLUENE (BHT), BUTYLATED HYDROXYANISOLE (BHA) AND SODIUM BISULFITE

ORGANIZATION:

ALTON OCHSNER MEDICAL FOUNDATION
1516 JEFFERSON HIGHWAY
NEW ORLEANS, LOUISIANA 70121
E.D. FROHLICH (504) 834-7070

TESTS PERFORMED:

FUNCTIONAL MONITORING -
ELECTROMAGNETIC
BLOOD FLOW DISTRIBUTION

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

EXPERIMENTAL HYPERTENSION

REMARKS:

CURRENTLY INVOLVED IN BLOOD FLOW MONITORING AND DEVELOPING NEW MONITORING TECHNIQUES IN LABORATORY ANIMALS AND HUMANS

ORGANIZATION:

BIODYNAMICS, INC.
METTLERS ROAD
EAST MILLSTONE, NEW JERSEY 08525
G. HOGAN (201) 873-2550

TEST PERFORMED:

FUNCTIONAL MONITORING -
ELECTROCARDIOGRAPHY (ECG)
INVASIVE PRESSURE MONITORING
MORPHOLOGY, LIGHT AND ELECTRON MICROSCOPY

TEST SYSTEMS UTILIZED:

DOGS, PRIMATES

COMPOUNDS TESTED:

THIS ORGANIZATION HAS STUDIED A NUMBER OF SUBSTANCES FOR VARIOUS CLIENTS.

ORGANIZATION:

CHICAGO COLLEGE OF OSTEOPATHIC MEDICINE
NUCLEAR MAGNETIC RESONANCE LABORATORY
5200 SOUTH ELLIS AVENUE
CHICAGO, ILLINOIS 60615
S.J. KOPP (312) 947-4698

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS
FUNCTIONAL MONITORING -
ELECTROCARDIOGRAPHY (ECG)
CARDIAC METABOLISM
MORPHOLOGICAL ALTERATIONS
BIOCHEMICAL MEASUREMENTS - PHOSPHORUS-31 NUCLEAR MAGNETIC RESONANCE

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

Cd, Mg, Ca AND OTHER BIOLOGICALLY ACTIVE CATIONS

REMARKS:

CURRENTLY DEVELOPING THE USE OF PHOSPHOROUS NMR TO MONITOR DYNAMIC CHANGES IN ENERGY METABOLISM IN THE MYOCARDIUM

ORGANIZATION:

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS
DEPARTMENTS OF PHARMACOLOGY AND ANATOMY
NEW YORK, NEW YORK 10032
A.L. WIT (212) 694-4197

TESTS PERFORMED:

FUNCTIONAL MONITORING
TISSUE EXPLANTS

TEST SYSTEMS UTILIZED:

DOGS

REMARKS:

CURRENTLY STUDYING MYOCARDIAL INFARCTION

ORGANIZATION:

EMORY UNIVERSITY
DEPARTMENT OF ANATOMY
ATLANTA, GEORGIA 30322
R.L. DEHAAN (404) 329-6237

TESTS PERFORMED:

CULTURED HEART CELLS -
ELECTRICAL PROPERTIES

TEST SYSTEMS UTILIZED:

MICE, CHICKENS

COMPOUNDS TESTED:

NEUROTOXINS

REMARKS:

CURRENT STUDIES CONCERN THE ELECTRICAL PROPERTIES OF THE MYOCARDIAL CELL

ORGANIZATION:

GENERAL MOTORS RESEARCH LABORATORIES
BIOMEDICAL SCIENCE DEPARTMENT
WARREN, MICHIGAN 48090
K.C. CHEN (313) 575-3484

TESTS PERFORMED:

PERFUSED HEART PREPARATION -
FUNCTIONAL AND BIOCHEMICAL MONITORING

TEST SYSTEMS UTILIZED:

RATS, RABBITS

COMPOUNDS TESTED:

CARBON MONOXIDE, NITROGEN

ORGANIZATION:

LOUISIANA STATE UNIVERSITY MEDICAL CENTER
DEPARTMENT OF ANATOMY
NEW ORLEANS, LOUISIANA 70119
F.H. KASTEN (504) 568-4011

TESTS PERFORMED:

CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

A NUMBER OF CARDIOACTIVE SUBSTANCES

ORGANIZATION:

MEDICAL COLLEGE OF GEORGIA
DEPARTMENT OF PHYSIOLOGY
AUGUSTA, GEORGIA 30902
V.T. WIEDMEIR (404) 828-3401

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS

TEST SYSTEMS UTILIZED:

GUINEA PIGS, RATS

COMPOUNDS TESTED:

CATECHOLAMINES, HISTAMINE, NITROGLYCERIN AND THEOPHYLLINE

REMARKS:

CURRENTLY EXAMINING THE HEART FROM THE STANDPOINT OF OXYGEN UTILIZATION AND THE DEPLETION OF HIGH ENERGY PHOSPHATE STORES

ORGANIZATION:

MICHIGAN STATE UNIVERSITY
DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY
EAST LANSING, MICHIGAN 48824
J.L. STICKNEY (517) 353-5479

TESTS PERFORMED:

FUNCTIONAL MONITORING -
ELECTROCARDIOGRAPHY (ECG)
MYOCARDIAL CONTRACTILE FORCE
SPONTANEOUS ACTIVITY OF RIGHT ATRIA
ARTERIAL BLOOD PRESSURE

TEST SYSTEMS UTILIZED:

DOGS, CATS, RATS, GUINEA PIGS, ETC.

COMPOUNDS TESTED:

1- -ACETYLMETHADOL (LAAM)

ORGANIZATION:

NATIONAL HEART AND LUNG INSTITUTE
SECTION OF PATHOLOGY
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20205
V.J. FERRANS (301) 496-5035

TESTS PERFORMED:

HISTOPATHOLOGIC - LIGHT AND ELECTRON MICROSCOPY

TEST SYSTEMS UTILIZED:

RATS, HAMSTERS, DOGS, SWINE, RABBITS, MICE, DUCKS

COMPOUNDS TESTED:

ADRIAMYCIN, Se-DEFICIENCY, EPINEPHRINE, NOREPINEPHRINE, CYCLOPHOSPHAMIDE, DAUNORUBICIN, MINOXIDIL

REMARKS:

CURRENT STUDIES CONCERN THE BLOCKING OF CARDIOTOXIC EFFECTS OF VARIOUS CHEMICAL AGENTS

ORGANIZATION:

NEW YORK MEDICAL COLLEGE
DEPARTMENT OF PHARMACOLOGY
MUNGER PAVILLION
VALHALLA, NEW YORK 10595
D. LEHR (914) 347-5855

TESTS PERFORMED:

BIOCHEMICAL MEASUREMENTS -
TISSUE ELECTROLYTES
ENZYMES
ENERGY METABOLISM

TEST SYSTEMS UTILIZED:

RATS, GUINEA PIGS, RABBITS AND DOGS

COMPOUNDS TESTED:

CATECHOLAMINES SUCH AS ISOPROTERENOL

REMARKS:

CURRENT STUDIES CONCERN BIOCHEMICAL MECHANISMS IN THE MYOCARDIUM

ORGANIZATION:

PENNSYLVANIA STATE UNIVERSITY
DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY PARK, PENNSYLVANIA 16802
R.L. McCARL (814) 865-1258

TESTS PERFORMED:

CULTURED HEART CELLS -
BEATING ACTIVITY
ATP TURNOVER RATE

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

HALOTHANE, PROPANOL, EPINEPHRINE

REMARKS:

R.L. McCARL HAS DEVELOPED A NEW AND HIGHLY SENSITIVE INSTRUMENTATION TO MONITOR THE RATE AND INTENSITY OF BEATING HEART CELLS

ORGANIZATION:

PURDUE UNIVERSITY SCHOOL OF VETERINARY MEDICINE
DEPARTMENT OF MICROBIOLOGY, PATHOLOGY AND PUBLIC HEALTH
WEST LAFAYETTE, INDIANA 47907
J.F. VAN VLEET (317) 494-5036

TESTS PERFORMED:

ULTRASTRUCTURAL CHANGES -
LIGHT AND ELECTRON MISCROSCOPY

TEST SYSTEMS UTILIZED:

BIRDS, DOGS, PIGS, RABBITS

COMPOUNDS TESTED:

SELENIUM DEFICIENCY, ADRIAMYCIN

REMARKS:

CURRENT STUDIES CONCERN ULTRASTRUCTURAL CHANGES AND PATHOLOGY IN CARDIOMYOPATHIES

ORGANIZATION:

STERLING-WINTHROP RESEARCH INSTITUTE
DEPARTMENT OF PHARMACOLOGY
RENSSELAER, NEW YORK 12144
A.A. ALOUSI (518) 445-8152

TESTS PERFORMED:

FUNCTIONAL MONITORING
- HEMODYNAMICS
- INVASIVE TECHNIQUES
- NON-INVASIVE TECHNIQUES

TISSUE EXPLANTS
PERFUSED HEART PREPARATION

TEST SYSTEMS UTILIZED:

RATS, CATS, DOGS, PRIMATES

COMPOUNDS TESTED:

CARDIOVASCULAR ACTIVE PHARMACEUTICAL AGENTS.

REMARKS:

R. PIWANKA, A. DEDEFELICE, T. SKULLEN ARE ALSO INVOLVED IN CARDIOVASCULAR TESTING AT THIS INSTITUTE.

ORGANIZATION:

THE CHICAGO MEDICAL SCHOOL
DEPARTMENT OF PHYSIOLOGY AND BIOPHYSICS
CHICAGO, ILLINOIS 60612
V.V. GLAVIANO AND M.T. PINDOK (312) 942-2771

TESTS PERFORMED:

FUNCTIONAL MONITORING
PERFUSED HEART PREPARATIONS
BIOCHEMICAL MEASUREMENTS

TEST SYSTEMS UTILIZED:

DOGS

COMPOUNDS TESTED:

ACETYLCHOLINE, NOREPINEPHRINE

REMARKS:

RESEARCH IS IN HYPERTENSION AND THE BIOCHEMICAL MECHANISMS INVOLVED IN HYPERTENSION

ORGANIZATION:

THE LILLY RESEARCH LABORATORIES
ELI LILLY AND COMPANY
INDIANAPOLIS, INDIANA 46206
H.R. SULLIVAN (317) 261-4631

TESTS PERFORMED:

FUNCTIONAL MONITORING -
ELECTROCARDIOGRAPHY (ECG)

TEST SYSTEMS UTILIZED:

DOGS

COMPOUNDS TESTED:

PROPOXYPHENE

ORGANIZATION:

UNIVERSITY OF CALIFORNIA
DEPARTMENT OF MEDICINE M-013
SAN DIEGO, LA JOLLA, CALIFORNIA 92093
S.E. MAYER (714) 452-4028

TESTS PERFORMED:

FUNCTIONAL MONITORING
TISSUE EXPLANTS

TEST SYSTEMS UTILIZED:

SEVERAL SMALL LABORATORY ANIMAL SPECIES

COMPOUNDS TESTED:

BUTOXAMINE, CATECHOLAMINES, PROSTAGLANDINS, PROPRANOLOL

REMARKS:

CURRENT STUDIES INVOLVE BETA-2 BLOCKING AGENTS AND THE PHYSIOLOGICAL EFFECTS OF OTHER CHEMICAL AGENTS

ORGANIZATION:

UNIVERSITY OF CALIFORNIA, LOS ANGELES
CENTER FOR THE HEALTH SCIENCES
LOS ANGELES, CALIFORNIA
M.W. SERAYDARIAN (213) 825-6892

TESTS PERFORMED:

CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

ADRIAMYCIN

REMARKS:

CURRENT STUDIES DEAL WITH ENERGY METABOLISM IN THE HEART

ORGANIZATION:

UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER
CARDIOVASCULAR AND PULMONARY RESEARCH LABORATORY
420 EAST 9TH AVE
DENVER, COLORADO 80262
R.F. GROVER AND L. HORWITZ (303) 394-8103

TESTS PERFORMED:

CARDIAC FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

DOGS

COMPOUNDS TESTED:

CATECHOLAMINES

REMARKS:

THE ORGANIZATION HAS AN EXTENSIVE PROGRAM FOR STUDYING MECHANISMS OF CARDIOVASCULAR DAMAGE

ORGANIZATION:

UNIVERSITY OF KANSAS
SCHOOL OF PHARMACY
DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY
LAWRENCE, KANSAS
D.G. WENZEL (913) 864-3591

TESTS PERFORMED:

CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

VARIOUS CARDIOTOXIC AGENTS

REMARKS:

D.G. WENZEL IS WORKING ON BOTH CULTURED HEART AND LUNG CELLS AND IS ALSO INVOLVED IN THE DEVELOPMENT OF CELL CULTURE TECHNIQUES

ORGANIZATION:

UNIVERSITY OF NORTH CAROLINA
DEPARTMENT OF MEDICINE
CHAPEL HILL, NORTH CAROLINA 27514
L.S. GETTES (606) 233-6106

TESTS PERFORMED:

TISSUE EXPLANTS -
ELECTROPHYSIOLOGICAL MONITORING
BIOCHEMICAL MONITORING

TEST SYSTEMS UTILIZED:

GUINEA PIGS, SWINE, DOGS

COMPOUNDS TESTED:

LIDOCAINE, QUINIDINE, TETRODOTOXIN

ORGANIZATION:

UNIVERSITY OF OKLAHOMA MEDICAL CENTER
OKLAHOMA CITY, OKLAHOMA 73190
L.B. HINSHAW (405) 325-0311

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS

TEST SYSTEMS UTILIZED:

DOGS

COMPOUNDS TESTED:

ENDOTOXIN

ORGANIZATION:

UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
DEPARTMENT OF PHYSIOLOGY
OKLAHOMA CITY, OKLAHOMA 73190
H.L. STONE (405) 271-2226

TESTS PERFORMED:

FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

DOGS, SWINE, MONKEYS

COMPOUNDS TESTED:

PROPRANOLOL, ISOPROTERNOL, NOREPINEPHRINE

REMARKS:

CURRENT STUDIES ALSO INVOLVE HYPERTENSION

ORGANIZATION:

UNIVERSITY OF OREGON
SCHOOL OF MEDICINE
DEPARTMENT OF PHARMACOLOGY
PORTLAND, OREGON
R. TANZ (503) 225-7805

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS -
BIOCHEMICAL MONITORING
FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

RATS, GUINEA PIGS, RABBITS, CATS

COMPOUNDS TESTED:

ACONITINE, OUABAIN, CALCIUM, EPINEPHRINE

ORGANIZATION:

UNIVERSITY OF PENNSYLVANIA
SCHOOL OF MEDICINE
JOHNSON RESEARCH FOUNDATION
PHILADELPHIA, PENNSYLVANIA 19174
C.H. BARLOW AND B. CHANCE (215) 243-8798

TESTS PERFORMED:

PERFUSED HEART -
MONITORING REDUCTIONS IN PYRIDINE NUCLEOTIDES
MITOCHONDRIAL METABOLISM

TEST SYSTEMS UTILIZED:

RATS, RABBITS, GUINEA PIGS

COMPOUNDS TESTED:

VARIOUS CARDIOACTIVE AGENTS

REMARKS:

CURRENTLY EXAMINING METABOLISM IN THE MITOCHONDRIA USING FLUOROMETRIC AND NMR TECHNIQUES

ORGANIZATION:

UNIVERSITY OF PENNSYLVANIA
SCHOOL OF VETERINARY MEDICINE
LABORATORIES OF PHARMACOLOGY
PHILADELPHIA, PENNSYLVANIA 19174
C.E. ARONSON (215) 243-5894

TESTS PERFORMED:

PERFUSED HEART -
MECHANICAL FUNCTIONAL MONITORING
BIOCHEMICAL FUNCTIONAL MONITORING
ELECTRICAL FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

SEVERAL CARDIOACTIVE SUBSTANCES

ORGANIZATION:

UNIVERSITY OF PENNSYLVANIA
SCHOOL OF VETERINARY MEDICINE
PHILADELPHIA, PENNSYLVANIA 19174
S. CHACKO (215) 243-8856

TESTS PERFORMED:

CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

CHICKENS, RATS

REMARKS:

THE DEVELOPMENTAL CHARACTERISTICS OF HEART CELLS ARE BEING EXAMINED

ORGANIZATION:

UNIVERSITY OF PENNSYLVANIA, THE GRADUATE HOSPITAL
DEPARTMENTS OF MEDICINE AND SURGERY
BOCKUS RESEARCH INSTITUTE
PHILADELPHIA, PENNSYLVANIA 19146
G. KARREMAN (215) 893-2377

TESTS PERFORMED:

FUNCTIONAL MEASUREMENTS -
VASCULAR REACTIVITY
SYSTOLIC EAR BLOOD PRESSURE
AORTIC STRIPS (THORACIC AORTA STRIPS)

TEST SYSTEMS UTILIZED:

RABBITS

COMPOUNDS TESTED:

CADMIUM ACETATE
CADMIUM CHLORIDE

ORGANIZATION:

UNIVERSITY OF SOUTH CAROLINA
SCHOOL OF MEDICINE
DEPARTMENT OF PHARMACOLOGY
COLUMBIA, SOUTH CAROLINA 29208
D.O. ALLEN (803) 777-7100

TESTS PERFORMED:

PERFUSED HEART -
CARDIAC METABOLISM AND CONTRACTION FORCE

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

CATECHOLAMINES

ORGANIZATION:

UNIVERSITY OF TEXAS
COLLEGE OF PHARMACY
AUSTIN, TEXAS 78712
D. ACOSTA (512) 471-4736

TESTS PERFORMED:

CULTURED HEART CELLS -
- MORPHOLOGY
- BEATING ACTIVITY
- CYTOPLASMIC ENZYME LEAKAGE
- LYSOSOMAL PERMEABILITY
- MITOCHONDRIAL FRAGILITY

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

SEVERAL SUBSTANCES SUCH AS NOREPINEPHRINE, COLCHICINE, DIAZEPAM, BUTYLATED HYDROXYTOLUENE, BUTYLATED HYDROXYANISOLE, ADRIAMYCIN

ORGANIZATION:

UNIVERSITY OF TEXAS
MEDICAL BRANCH
DEPARTMENT OF PATHOLOGY
GALVESTON, TEXAS 77550
P.J. BOOR (713) 765-3656

TESTS PERFORMED:

HISTOPATHOLOGICAL, ULTRASTRUCTURAL, HISTOCHEMICAL AND BIOCHEMICAL CHANGES - HOMOGENIZED TISSUES, METABOLISM ACTIVITY OF HOMOGENATE

TEST SYSTEMS UTILIZED:

RATS, MICE, IN VITRO ORGAN HOMOGENATES

COMPOUNDS TESTED:

ALLYLAMINE, ARIAMYCIN, ISOPROTERENOL, OTHER ALIPHATIC AMINES

ORGANIZATION:

UNIVERSITY OF VIRGINIA
SCHOOL OF MEDICINE
DEPARTMENT OF PHYSIOLOGY
CHARLOTTESVILLE, VIRGINIA 22908
R.M. BERNE, R. RUBIO (804) 924-5108

TESTS PERFORMED:

FUNCTIONAL MONITORING -
- CORONARY CIRCULATION
- CARDIAC METABOLISM
- RADIONUCLEOTIDE METABOLISM

CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

DOGS, RABBITS, GUINEA PIGS

COMPOUNDS TESTED:

ADENOSINE METABOLISM INHIBITORS

ORGANIZATION:

UNIVERSITY OF VIRGINIA
SCHOOL OF MEDICINE
DEPARTMENT OF PHYSIOLOGY
CHARLOTTESVILLE, VIRGINIA 22903
N. SPERELAKIS (804) 924-2655

TESTS PERFORMED:

CULTURED HEART CELLS -
- MORPHOLOGICAL MONITORING
- BIOCHEMICAL MONITORING
- PHYSIOLOGICAL FUNCTIONAL MONITORING

MUSCLE EXPLANTS
PERFUSED HEART PREPARATIONS

TEST SYSTEMS UTILIZED:

CHICKENS, RATS, GUINEA PIGS, DOGS

COMPOUNDS TESTED:

ISOPROTERENOL, METHYLXANTHINES, ANGIOTENSIN, LIDOCAINE, PROCAINE, BIOLOGICALLY ACTIVE CATIONS AND NUMEROUS OTHER SUBSTANCES

REMARKS:

CURRENTLY INVOLVED IN THE DEVELOPMENT OF CULTURED HEART CELLS, ORGAN CULTURES AND IN DESCRIBING DAMAGE TO THESE TEST SYSTEMS CAUSED BY CHEMICAL AGENTS

ORGANIZATION:

U.S. AIR FORCE AEROSPACE MEDICAL RESEARCH LABORATORY
TOXIC HAZARDS DIVISION
WRIGHT-PATTERSON AIR FORCE BASE, OHIO
K.C. BACK (513) 255-3916

TESTS PERFORMED:

TISSUE EXPLANTS -
ISOLATED ATRIA: CONTRACTILITY, BIOCHEMISTRY

TEST SYSTEMS UTILIZED:

DOG, GUINEA PIGS, RATS

COMPOUNDS TESTED:

BROMOCHLORODIFLUOROMETHANE (BCF) FLUOROCARBONS

ORGANIZATION:

U.S. ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASES
FORT DETRICK
FREDERICK, MARYLAND 21701
C.T. LIU (301) 663-2148

TESTS PERFORMED:

FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

REHESUS MACQUE, DOGS, RABBITS

COMPOUNDS TESTED:

VIRAL AND RICKETTSIAL TOXINS

REMARKS:

THE EFFECTS OF VIRAL AND RICKETTSIAL DISEASE TOXINS ON THE HEART ARE BEING EXAMINED

ORGANIZATION:

U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE
ALTITUDE RESEARCH DIVISION
NATICK, MASSACHUSETTS 01760
R.L. BURSE (617) 653-1000 Ext. 2851

TESTS PERFORMED:

FUNCTIONAL MONITORING -
CARDIAC OUTPUT
LEFT VENTRICULAR END-DIASTOLIC PRESSURE

TEST SYSTEMS UTILIZED:

GOATS, RATS, MICE, DOGS

COMPOUNDS TESTED:

HYPOXIA

REMARKS:

CURRENT STUDIES CONCERN THE EFFECTS OF HYPOXIA INDUCED BY HIGH ALTITUDE ON THE HEART AND OTHER ORGAN FUNCTIONS

ORGANIZATION:

U.S. FOOD AND DRUG ADMINISTRATION
BUREAU OF DRUGS
DRUG BIOLOGY DIVISION
WASHINGTON, D.C.
W.C. VANARSDEL (202) 443-4730

TESTS PERFORMED:

FUNCTIONAL MONITORING -
ELECTROCARDIOGRAPHY (ECG)

TEST SYSTEMS UTILIZED:

RATS, CATS, DOGS, RABBITS, PIGS, HAMSTERS

COMPOUNDS TESTED:

ISOPROTERINOL, ADRIAMYCIN

REMARKS:

W.C. VANARSDEL HAS EXAMINED THE ECG'S FROM APPROXIMATELY 600 ANIMALS TO SEE IF EARLY MYOCARDIAL DEGENERATIVE CHANGES CAN BE DETECTED IN ANIMALS.

G.L. JOHNSON, S.J. EHRREICH AND J.A. VICK ARE ALSO INVOLVED IN CARDIOVASCULAR TESTING AT THIS ORGANIZATION.

ORGANIZATION:

U.S. FOOD AND DRUG ADMINISTRATION
DIVISION OF DRUG BIOLOGY
HEW
WASHINGTON, D.C. 20204
T. BALAZS, E.H. HERMAN (202) 245-1357

TESTS PERFORMED:

HISTOPATHOLOGICAL AND MORPHOLOGICAL ALTERATIONS
FUNCTIONAL MONITORING
BIOCHEMICAL MEASUREMENTS

TEST SYSTEMS UTILIZED:

VARIOUS SMALL LABORATORY ANIMALS

COMPOUNDS TESTED:

A NUMBER OF CARDIOACTIVE SUBSTANCES

REMARKS:

CURRENTLY INVOLVED IN AN EXTENSIVE PROGRAM FOR THE MONITORING OF THE CARDIOVASCULAR EFFECTS OF DRUGS

ORGANIZATION:

WASHINGTON UNIVERSITY
DEPARTMENT OF MEDICINE
HYPERTENSION DIVISION
915 N. GRAND BLVD., BUILDING 3
ST. LOUIS, MISSOURI 63108
H.M. PERRY (314) 652-4100 Ext. 555

TESTS PERFORMED:

PERFUSED HEART PREPARATIONS

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

TRACE METALS

REMARKS:

CURRENT STUDIES CONCERN CARDIAC METABOLISM

ORGANIZATION:

WAYNE STATE UNIVERSITY
SCHOOL OF MEDICINE
DEPARTMENT OF PHYSIOLOGY
DETROIT, MICHIGAN 48201
D.G. PENNEY (313) 577-1539

TESTS PERFORMED:

FUNCTIONAL MONITORING - WHOLE ANIMAL: HEART AND CIRCULATION

TEST SYSTEMS UTILIZED:

RATS

COMPOUNDS TESTED:

CARBON MONOXIDE

REMARKS:

D.G. PENNEY IS DEVELOPING PROCEDURES FOR BETTER FUNCTIONAL MONITORING

APPENDIX A

INDEX OF TESTS PERFORMED BY EACH ORGANIZATION

BIOCHEMICAL MEASUREMENTS

Chicago College of Osteopathic Medicine
The Chicago Medical School
New York Medical College
University of Virginia
U.S. Food and Drug Administration

CULTURED HEART CELLS

Allied Chemical
Emory University
Louisiana State University Medical Center
Pennsylvania State University
University of Kansas
University of Pennsylvania, School of Veterinary Medicine
University of California, Los Angeles
University of Texas
University of Virginia

FUNCTIONAL MEASUREMENTS

Allied Chemical
Alton Ochsner Medical Foundation
Biodynamics, Inc.
Chicago College of Osteopathic Medicine
The Chicago Medical School
Columbia University College of Physicians and Surgeons
The Lilly Research Laboratories
Michigan State University
Sterling Winthrop Research Institute
University of California, La Jolla
University of Colorado Health Sciences Center
University of Oklahoma Health Sciences Center
University of Pennsylvania, The Graduate Hospital
University of Virginia
U.S. Army Medical Research Institute of Infectious Diseases
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration
Wayne State University School of Medicine

MORPHOLOGICAL MEASUREMENTS

Biodynamics, Inc.
Chicago College of Osteopathic Medicine
National Heart and Lung Institute
Purdue University
University of Texas Medical Branch
U.S. Food and Drug Administration

TISSUE EXPLANTS AND PERFUSED HEART PREPARATIONS

Allied Chemical
Chicago College of Osteopathic Medicine
The Chicago Medical School
Columbia University College of Physicians and Surgeons
General Motors Research Laboratories
Medical College of Georgia
Sterling Winthrop Research Institute
University of California, La Jolla
University of North Carolina
University of Oklahoma Medical Center
University of Oregon
University of Pennsylvania, School of Medicine
University of Pennsylvania, School of Veterinary Medicine
University of South Carolina
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory
Washington University

APPENDIX B

INDEX OF TEST SYSTEMS UTILIZED

BY EACH ORGANIZATION

CATS

Michigan State University
Sterling-Winthrop Research Institute
University of California
University of Oregon
U.S. Food and Drug Administration

Biochemical Measurements
U.S. Food and Drug Administration

Functional Measurements
Michigan State University
Sterling-Winthrop Research Institute
University of California
U.S. Food and Drug Administration

Morphological Measurements
U.S. Food and Drug Administration

Perfused Heart Preparations
Sterling-Winthrop Research Institute
University of Oregon

Tissue Explants
Sterling-Winthrop Research Institute
University of California

CHICKENS

Emory University
Purdue University
University of Pennsylvania, School of Veterinary Medicine
University of Virginia

Cultured Heart Cells
Emory University
University of Pennsylvania, School of Veterinary Medicine
University of Virginia

Morphological Measurements
Purdue University

Perfused Heart Preparations
University of Virginia

Tissue Explants
University of Virginia

DOGS

Army Medical Research Institute of Infectious Diseases
The Chicago Medical School
Columbia University College of Physicians and Surgeons
The Lilly Research Laboratories
Michigan State University
National Heart and Lung Institute
New York Medical College
Purdue University
Sterling-Winthrop Research Institute
University of California
University of Colorado Health Science Center
University of North Carolina
University of Oklahoma Medical Center
University of Oklahoma Health Sciences Center
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory
U.S. Food and Drug Administration

Biochemical Measurements
The Chicago Medical School
New York Medical College
U.S. Food and Drug Administration

Cultured Heart Cells
University of Virginia

Functional Measurements
Biodynamics, Inc.
The Chicago Medical School
Columbia University College of Physicians and Surgeons
The Lilly Research Laboratories
Michigan State University
Sterling-Winthrop Research Institute
University of California
University of Colorado Medical Center
University of Oklahoma Health Sciences Center
University of Virginia
U.S. Army Medical Research Institute of Infectious Diseases
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration

Morphological Measurements
Biodynamics, Inc.
National Heart and Lung Institute
Purdue University
U.S. Food and Drug Administration

DOGS (Continued)

Perfused Heart Preparations
Sterling-Winthrop Research Institute
The Chicago Medical School
University of Oklahoma Medical Center
University of Virginia

Tissue Explants
Columbia University of College of Physicians and Surgeons
Sterling-Winthrop Research Institute
University of California
University of North Carolina
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory

DUCKS

National Heart and Lung Institute

Morphological Measurements
National Heart and Lung Institute

GOATS

U.S. Army Research Institute of Environmental Medicine

Functional Measurements
U.S. Army Research Institute of Environmental Medicine

GUINEA PIGS

Medical College of Georgia
Michigan State University
New York Medical College
University of California
University of North Carolina
University of Oregon
University of Pennsylvania, School of Medicine
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory
U.S. Food and Drug Administration

Biochemical Measurements
New York Medical College
U.S. Food and Drug Administration

Cultured Heart Cells
University of Virginia

Functional Measurements
Michigan State University
University of California
University of Virginia
U.S. Food and Drug Administration

GUINEA PIGS (Continued)

Morphological Measurements
U.S. Food and Drug Administration

Perfused Heart Preparation
Medical College of Georgia
University of Oregon
University of Pennsylvania, School of Medicine
University of Virginia

Tissue Explants
University of California
University of North Carolina
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory

HAMSTERS

National Heart and Lung Institute
U.S. Food and Drug Administration

Functional Measurements
U.S. Food and Drug Administration

Morphological Measurements
National Heart and Lung Institute

MICE

Emory University
National Heart and Lung Institute
University of California
University of Texas, Medical Branch
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration

Biochemical Measurements
U.S. Food and Drug Administration

Cultured Heart Cells
Emory University

Functional Measurements
University of California
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration

MICE (Continued)

Morphological Measurements
National Heart and Lung Institute
University of Texas, Medical Branch
U.S. Food and Drug Adminstration

Tissue Explants
University of California

MONKEYS

Sterling-Winthrop Research Institute
University of Oklahoma Health Sciences Center
U.S. Army Medical Research Institute of Infectious Diseases

Functional Measurements
Sterling-Winthrop Research Institute
University of Oklahoma Health Sciences Center
U.S. Army Medical Research Institute of Infectious Diseases

Perfused Heart Preparations
Sterling-Winthrop Research Institute

Tissue Explants
Sterling-Winthrop Research Institute

PIGS

Purdue University
University of North Carolina
University of Oklahoma Health Sciences Center
U.S. Food and Drug Administration

Functional Measurements
University of Oklahoma Health Sciences Center

Morphological Measurements
Purdue University

Tissue Explants
University of North Carolina

RABBITS

General Motors Research Laboratories
National Heart and Lung Institute
New York Medical College
Purdue University
University of California
University of Oregon
University of Pennsylvania, School of Medicine

RABBITS (Continued)

University of Pennsylvania, The Graduate Hospital
University of Virginia
U.S. Army Medical Research Institute of Infectious Diseases
U.S. Food and Drug Administration

Biochemical Measurements
New York Medical College
University of Chicago
U.S. Food and Drug Administration

Cultured Heart Cells
University of Virginia

Functional Measurements
University of California
University of Pennsylvania, The Graduate Hospital
University of Virginia
U.S. Army Medical Research Institute of Infectious Diseases
U.S. Food and Drug Administration

Morphological Measurements
National Heart and Lung Institute
Purdue University
U.S. Food and Drug Administration

Perfused Heart Preparations
General Motors Research Laboratories
University of Oregon
University of Pennsylvania, School of Medicine

Tissue Explants
University of California

RATS

Alton Ochsner Medical Foundation
Chicago College of Osteopathic Medicine
General Motors Research Laboratories
Louisiana State University Medical Center
Medical College of Georgia
Michigan State University
National Heart and Lung Institute
New York Medical College
Pennsylvania State University
Shell Development TX 141
Sterling-Winthrop Research Institute
University of California

RATS (Continued)

University of Kansas
University of Oregon
University of Pennsylvania, School of Medicine
University of Pennsylvania, School of Veterinary Medicine
University of South California
University of California, Los Angeles
University of Texas
University of Texas, Medical Branch
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration
Washington University
Wayne State University

Biochemical Measurements
New York Medical College
University of Chicago
U.S. Food and Drug Administration

Cultured Heart Cells
Louisiana State University Medical Center
Pennsylvania State University
Shell Development, TX 141
University of Kansas
University of Pennsylvania
University of Southern California
University of Texas
University of Virginia

Functional Measurements
Alton Ochsner Medical Foundation
Chicago College of Osteopathic Medicine
Michigan State University
Shell Development, TX 141
Sterling-Winthrop Research Institute
University of California
U.S. Army Research Institute of Environmental Medicine
U.S. Food and Drug Administration
Wayne State University

Morphological Measurements
Chicago College of Osteopathic Medicine
National Heart and Lung Institute
University of Texas, Medical Branch
U.S. Food and Drug Administration

RATS (Continued)

Perfused Heart Preparations

Chicago College of Osteopathic Medicine
General Motors Research Laboratories
Medical College of Georgia
Shell Development, TX 141
Sterling-Winthrop Research Institute
University of Oregon
University of Pennsylvania, School of Medicine
University of Pennsylvania, School of Veterinary Medicine
University of South Carolina
University of Virginia
Washington University
Wayne State University

Tissue Explants

Sterling-Winthrop Research Institute
University of California
University of Virginia
U.S. Air Force Aerospace Medical Research Laboratory

APPENDIX C

INDEX OF INDIVIDUALS IN THE DIRECTORY

NAME	ORGANIZATION
Acosta, D.	University of Texas at Austin College of Pharmacy
Allen, D.O.	University of South Carolina
Alousi, A.A.	Sterling Winthrop Research Institute
Aronson, C.E.	University of Pennsylvania School of Veterinary Medicine
Back, K.C.	U.S. Air Force Aerospace Medical Research Laboratory, Ohio
Balazs, T.	U.S. Food and Drug Administration
Barlow, C.H.	University of Pennsylvania School of Medicine
Berne, R.M.	University of Virginia
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Burse, R.L.	U.S. Army Research Institute of Environmental Medicine
Chacko, S.	University of Pennsylvania School of Veterinary Medicine
Chance, B.	University of Pennsylvania School of Medicine
Chen, K.C.	General Motors Research Laboratories
Dedefelice, A.	Sterling Winthrop Research Institute
Dehaan, R.L.	Emory University
Ehrreich, S.J.	U.S. Food and Drug Administration
Ferrans, V.J.	National Heart and Lung Institute
Frohlich, E.D.	Alton Ochsner Medical Foundation
Gad, S.C.	Allied Chemical

NAME	ORGANIZATION
Gettes, L.S.	University of North Carolina
Glaviano, V.V.	The Chicago Medical School
Grover, R.F.	University of Colorado Health Sciences Center
Herman, E.H.	U.S. Food and Drug Administration
Hinshaw, L.B.	University of Oklahoma Medical Center
Hogan, G.	Biodynamics, Inc.
Horwitz, L.	University of Colorado Health Sciences Center
Johnson, G.L.	U.S. Food and Drug Administration
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Pindok, M.T.	The Chicago Medical School
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Rubio, R.	University of Virginia

NAME	ORGANIZATION
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Skullen, T.	Sterling Winthrop Research Institute
Sperelakis, N.	University of Virginia
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Stone, H.L.	University of Oklahoma Health Sciences Center
Sullivan, H.R.	The Lilly Research Laboratories
Tanz, R.	University of Oregon
Van Arsdel, Wm. C. III	U.S. Food and Drug Administration
Van Vleet, J.F.	Purdue University
Vick, J.A.	U.S. Food and Drug Administration
Wenzel, D.G.	University of Kansas
Wiedmeir, V.T.	Medical College of Georgia
Wit, A.L.	Columbia University College of Physicians and Surgeons

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