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EVALUATION OF SHORT-TERM BIOASSAYS $\ensuremath{\S{}}$ TO PREDICT FUNCTIONAL IMPAIRMENT

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

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Richard Thomas Purna Greenaway

October 1980

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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 <u>in vivo</u> and <u>in vitro</u> techniques. The <u>in vivo</u> 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 <u>in vitro</u> 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.

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EXECUTIVE SUMMARY

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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, <u>Evaluation of Short-Term Bioassays to Predict Functional</u> <u>L Impairment: Selected Short-Term Cardiovascular Toxicity Tests.</u>

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 <u>in vitro</u>); 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

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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, <u>Selected Short-Term</u> 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, <u>Selected Short-Term Cardiovascular Toxicity Tests</u>.

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1.

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.

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

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

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TESTS PERFORMED:

PERFUSED HEART PREPARATIONS CULTURED MYOCARDIAL CELLS WHOLE ANIMAL FUNCTIONAL MONITORING

TEST SYSTEMS UTILIZED:

RATS

Strate of Character

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COMPOUNDS TESTED:

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

11

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FRECEDING FANE BLANK-NOT FILMER

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:

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

A BRITER BERT

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:

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

E

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:

5

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

Se the Party of the work

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:

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CURRENTLY STUDYING MYOCARDIAL INFARCTION

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Se NOTIFICATION TOP

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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:

1.1.1.1

CURRENT STUDIES CONCERN THE ELECTRICAL PROPERTIES OF THE MYOCARDIAL CELL

A REPORT OF THE AND A

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

17

ALANS STREETS WE THE S

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

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COMPOUNDS TESTED:

A NUMBER OF CARDIOACTIVE SUBSTANCES

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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

1.1.1

52 T

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)

A. A.

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

NEW YORK MEDICAL COLLEGE DEPARTMENT OF PHARMACOLOGY MUNGER PAVILLION VALHALLA, NEW YORK 10595 D. LEHR (9:4) 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

22

Market Market

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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 INSTRU-MENTATION TO MONITOR THE RATE AND INTENSITY OF BEATING HEART CELLS

23

State State State

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:

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CURRENT STUDIES CONCERN ULTRASTRUCTURAL CHANGES AND PATHOLOGY IN CARDIOMYOPATHIES

24

Sa REPORT OF THE COM

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:

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

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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:

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RESEARCH IS IN HYPERTENSION AND THE BIOCHEMICAL MECHANISMS INVOLVED IN HYPERTENSION

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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

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COMPOUNDS TESTED:

PROPOXY PHENE

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:

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

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:

L'ET L'ALLER

CURRENT STUDIES DEAL WITH ENERGY METABOLISM IN THE HEART

29

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:

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

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Se THE CONTRACTOR OF ST

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:

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

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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

32

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Non-States

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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

AND THE REPORT OF THE STAR

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:

121

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CURRENT STUDIES ALSO INVOLVE HYPERTENSION

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A. 198

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:

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ACONITINE, OUABAIN, CALCIUM, EPINEPHRINE

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UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE JOHNSON RESEARCH FOUNDATION PHILADELPHIA, PENNSYLVANIA 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:

STOR.

CURRENTLY EXAMINING METABOLISM IN THE MITOCHONDRIA USING FLUOROMETRIC AND NMR TECHNIQUES

36

Jan ma
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

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COMPOUNDS TESTED:

SEVERAL CARDIOACTIVE SUBSTANCES

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CASIMON CONT

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

38

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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:

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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:

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CATECHOLAMINES

Mary multiple

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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

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COMPOUNDS TESTED:

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

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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

SA BELLEVILLE THE STREET

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

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TESTS PERFORMED:

FUNCTIONAL MONITORING -CORONARY CIRCULATION CARDIAC METABOLISM RADIONUCLEOTIDE METABOLISM CULTURED HEART CELLS

TEST SYSTEMS UTILIZED:

DOGS, RABBITS, GUINEA PIGS

COMPOUNDS TESTED:

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ADENOSINE METABOLISM INHIBITORS

43

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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

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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

45

APPRIL TO BE MERCER STORE

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:

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

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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:

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

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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.

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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

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REMARKS:

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1

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

49

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So the Case of the

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:

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CURRENT STUDIES CONCERN CARDIAC METABOLISM

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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:

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

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APPENDIX A

INDEX OF TESTS PERFORMED BY EACH ORGANIZATION

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BIOCHEMICAL MEASUREMENTS

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

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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

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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

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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

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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

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APPENDIX B

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INDEX OF TEST SYSTEMS UTILIZED

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