OMNIBUS SOLICITATION OF THE NATIONAL INSTITUTES OF HEALTH, CENTERS FOR DISEASE CONTROL AND PREVENTION, AND FOOD AND DRUG ADMINISTRATION FOR

SMALL BUSINESS INNOVATION RESEARCH (SBIR)

AND

SMALL BUSINESS TECHNOLOGY TRANSFER (STTR)

GRANT APPLICATIONS

NIH, CDC, and FDA Program Descriptions and Research Topics

SUBMISSION DATES

APRIL 1, AUGUST 1, AND DECEMBER 1, 2006

National Institutes of Health (SBIR and STTR)

Centers for Disease Control and Prevention (SBIR)

Food and Drug Administration (SBIR)

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Funding Opportunity Announcements, Application Instructions, and Appendices are contained in separate files. Follow the links below to view these documents.

FUNDING OPPORTUNITY ANNOUNCEMENTS

SMALL BUSINESS INNOVATION RESEARCH PROGRAM PARENT ANNOUNCEMENT (SBIR [R43/R44])
HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-06-120.HTML

SMALL BUSINESS TECHNOLOGY TRANSFER PROGRAM PARENT ANNOUNCEMENT (STTR [R41/R42])
HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-06-121.HTML

ADDITIONAL SPECIAL ANNOUNCEMENTS FOR SMALL BUSINESS RESEARCH OPPORTUNITIES
HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIR_ANNOUNCEMENTS.HTM

APPLICATION INSTRUCTIONS

APPLICATION INSTRUCTIONS
(HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/424/SF424_RR_GUIDE_SBIR_STTR.DOC)

SF424 (R&R) APPLICATION AND ELECTRONIC SUBMISSION INFORMATION
(HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/424/INDEX.HTM)

APPENDICES

STTR MODEL AGREEMENT (MS WORD)

EXTRAMURAL INVENTION REPORTING COMPLIANCE RESPONSIBILTIES (PDF)

NIH SBIR/STTR INTERNET GUIDE (MS WORD)

PROGRAM DESCRIPTIONS AND RESEARCH GRANT TOPICS

The research topics shown in this solicitation represent program areas that may be of interest to applicant small business concerns in the development of projects that have potential for commercialization. Small business concerns are encouraged to submit SBIR/STTR grant applications in these areas.

APPLICABLE TO NIH ONLY: SBIR and STTR grant applications will be accepted and considered in any area within the mission of the awarding components identified in this solicitation.

Applicants are strongly encouraged to query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, and FDA awarding components.

Additional information on each of the awarding components and their research interests is available electronically on the home pages shown throughout the "Research Topics" section of the solicitation.

The Fogarty International Center, which provides support only for conferences, postdoctoral fellowships for research in the United States and abroad, and senior scientist exchanges between the United States and other countries, does not participate in the SBIR/STTR program.

NATIONAL INSTITUTES OF HEALTH (NIH)

The mission of the NIH is to improve human health through biomedical and behavioral research, research training, and communications. The programs of the NIH are oriented principally towards basic and applied scientific inquiry related to the causes, diagnosis, prevention, treatment, and rehabilitation of human diseases and disabilities; the fundamental biological processes of growth, development, and aging; and the biological effects of the environment. In addition, the NIH sponsors training of research personnel; career development of new and established scientists; evaluation and dissemination of new information about medicine and health; construction and renovation of research facilities and provision of other research resources; and improvements in biomedical communications.

To carry out these responsibilities, the NIH is organized into awarding components (Institutes/Centers). Those components that have an extramural element, that is, provide funds for research and research training activities in organizations external to the NIH, are shown below. The NIH makes every effort to finance worthy proposals, including the co-funding of such proposals by one or more awarding components having relevance in the projects.

TRANS-NIH RESEARCH PROGRAMS

Phase II Competing Renewal Awards

Some NIH Institutes/Centers (ICs) now offer Phase II SBIR/STTR awardees the opportunity to apply for a Phase II Competing Renewal award. Some ICs have announced this opportunity through the NIH Guide for Grants and Contracts (see list below), and some are using this Omnibus SBIR/STTR Grant Solicitation. Only those small business concerns who have been awarded a Phase II are eligible to apply for a Phase II Competing Renewal award. Moreover, this opportunity is only for Phase II awardees that propose to continue the process of assessing and improving drugs or devices or propose to conduct preclinical studies of drugs or devices that ultimately require: 1) clinical evaluation, 2) approval of a Federal regulatory agency, and/or 3) continuing refinements to durable medical equipment (DME) designs such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards. Such products include, but are not limited to, devices, drugs, vaccines, therapeutics, and medical implants related to the mission of the IC. The product being developed must be one for which Federal regulatory approval (e.g., FDA) is a required step toward commercialization. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Competing Renewal application. Additional requirements and instructions (e.g., submission of a letter of intent) are available in the specific IC research topics section and in the specific IC Program Announcements (http://grants.nih.gov/grants/funding/sbir_announcements.htm). The following NIH ICs will accept applications for Phase II Competing Renewal awards: **NIAAA, NIA, NIAID**, **NICHD, NIDA** (SBIR only), **NIMH** (SBIR only), **NHLBI** (SBIR only and only Competing Renewals of NHLBI-supported Phase II awards), **NIDCD, NIDDK, and NINDS.**

Bioengineering Nanotechnology Initiative

See Program Announcement at http://grants.nih.gov/grants/guide/pa-files/PA-06-009.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-008.html (STTR)

The NIH invites grant applications for nanotechnologies useful to biomedicine. Nanotechnology is defined as the creation of functional materials, devices and systems through control of matter at the scale of 1 to 100 nanometers, and the exploitation of novel properties and phenomena at the same scale. Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine. Moreover, nanotechnologies developed in the next several years may well form the foundation of significant commercial platforms.

The following list describes some of the priority areas for nanoscience and nanotechnology research support at NIH. The list is not exhaustive, nor are the topics mutually exclusive. Their presentation here exemplifies important scientific areas in which research at the nanoscale has the potential to make enormous contributions to solving biomedical problems.

- Nanomaterials (enabling): development of synthetic nanoscale building blocks for the formulation of bottom-up approaches to complex and multi-functional nano materials. These materials are expected to find use in applications towards pharmaceutical delivery, towards the development of contrast and biological agents, and multi-functional medical devices.
- Nano-bio interfaces: science of controlling the interface between biomolecular systems and nanoscale synthetic materials, which involves ability to control the interface architecture and transduction of the control signal through this interface.
- Nanoimaging: real-time imaging of subcellular structure, function, properties and metabolism.
- Cell biology: nano-scale research on cellular processes, including biophysics of molecular assemblies, membranes, organelles, and macromolecules.
- Molecular and cellular sensing/signaling: technologies to detect biological signals and single molecules within and outside cells.
- Prosthetics: mechanical, chemical, and cellular implant nano-technologies to achieve functional replacement tissue architectures.
- Environmental and health impact of nanotechnologies: ramifications of nanomaterial processing, use, and degradation on health and the environment.
- In-vivo therapeutics: development of nanoparticles that enable controlled release of therapeutic agents, antibodies, genes and vaccines into targeted cells.
- Sensor technologies: detection and analysis of biologically relevant molecular and physical targets in samples from blood, saliva and other body fluids, or for use in the research laboratory (purified samples), clinical specimens, and in the living body.
- Nanosystem design and application: fundamental principles and tools to measure and image the biological processes of health and disease and methods to assemble nanosystems.
- Bioinformatics for nanotechnology: algorithms and computer software to enable and support all of the above.

Manufacturing Processes of Medical, Dental, and Biological Technologies (STTR [R41/R42])

http://grants.nih.gov/grants/guide/pa-files/PA-06-012.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-013.html (STTR)

The NIH encourages research related to advanced processing in the manufacture of biomedical products and the implementation of new technologies in medical care. New methods, procedures, measures, and controls are needed for manufacturing a broad range of technologies and products with unsurpassed quality and to lower manufacturing costs for existing and/or new processes. Research is also encouraged that can contribute to the containment and reduction of health care costs and that can improve the cost

effectiveness, quality, and accessibility of the health care system.

Because manufacturing-related R&D is extremely broad in scope, the following examples of research topics may be of interest but are not meant to be exhaustive.

Flexible computer-assisted integrated manufacturing equipment and intelligent processing equipment adaptable to the varied needs of biomedical research and medical care device and material production.

Systems engineering and management tools needed for the development of biomedical product manufacturing plants with particular emphasis on the requirements to meet GMP requirements for FDA approvals.

Technology for the manufacture of research instrumentation, such as highly sensitive, high resolution spectrometers, highly selective electrodes, microarray devices, and microfluidic devices.

Technology for the manufacture of clinical diagnostic devices and reagents.

Technology for the manufacture of novel diagnostic imaging devices for both invasive and non-invasive techniques.

Technology for the manufacture and delivery of therapeutic drugs, including for example, synthetic process chemistry, separations methods, formulation, and dosage delivery.

Technology for the manufacture of implantable devices and materials, including drug delivery pumps, prosthetic organs, artificial tissues, electronic sensors and electrical stimulators.

Technology for the production of natural products derived from plant, animal, and microbial sources, such as antibiotics, anticancer drugs, and other therapeutic agents, and useful synthetic starting materials.

Technology for the production and isolation of biotechnology products, such as proteins, antibodies, nucleic acids, vaccines, and vectors for genetic engineering and gene therapy.

Technology for the production of new materials relevant to biomedical research and medical care delivery, including nanomaterials, carbon fibers, polymeric materials, self-assembled monolayers, controlled size, shape, and porosity particles, filters, membranes, silicon substrates for microarrays, superconducting materials for NMR and MRI magnets, and implantable magnetic materials for external magnetic manipulation.

Technology for manufacture of medical device power sources, such as high energy density, long life-time batteries, solar cells, and fuel cells.

Technology for the fabrication of medical care instruments and devices such as minimally invasive and magnetic field tolerant surgical instruments, orthopedic implants, prostheses, and enabling devices for the injured and disabled.

Rapid prototyping and manufacture technology suitable for remote site and on demand production processes.

Technology to promote the recovery, reuse, and remanufacture (recycling) of medical materials and equipment.

Technology for the manufacture of biomedically specialized computational and information technology equipment and software.

Development of innovative products that facilitate the safety and health training of hazardous materials workers, emergency responders, and skilled support personnel. (See also NIEHS Worker Education and Training Program at http://www.niehs.nih.gov/wetp/home.htm.)

Development of Synthetic and Natural Biomaterial Reference Materials

The NIH invites applications for the development of synthetic or natural biomaterial reference materials (RMs). RMs are used for standardization of studies of interactions between materials and blood and tissues, for calibration of physicochemical test methods, and/or for reference controls in physical, chemical, and materials structure characterization tests. All innovative developments of biomaterials and devices also need measurements to demonstrate their innovation and improvement. Because RMs lie at the heart of measurement technology, funding for their development could play a key role in future advances in biomaterials and biomedical material device technologies.

Industry uses biomaterial RMs for quality assurance and traceability. The Food and Drug Administration considers them useful for comparing new

biomaterials, or new uses of biomaterials, with existing standards and materials. In order to have maximum utilitarian value, it is intended that these biomaterial RMs be stored at, and distributed by, the National Institute of Standards and Technology (NIST). Hence, they must be produced to meet the stringent requirements of the NIST Standard Reference Material Program. *It is important for applicants to contact NIST (Dr. John A. Tesk, (301) 975-6799; Email: john.tesk@nist.gov) to obtain detailed information on requirements of that program prior to preparing and submitting their applications.*

Biomaterial RMs may be synthetic polymers, ceramics, metals, or mixtures of these, or may be derived from living tissues. The choice of RM to be developed is up to the applicant but must be fully justified based on the applicant's knowledge of the magnitude of the current or potential utilization of the biomaterial. RMs of known particular value include: (1) silica-filled poly(dimethylsiloxane), (2) aliphatic polyether urethane, (3) poly (vinylchloride), (4) poly(methylmethacrylate), (5) expanded poly (tetrafluoroethylene) of varying standardized internodal distances, (6) oxygen permeability standards, and (7) carbon materials used in mechanical heart valve designs.

RMs must be of appropriate size and shape. The form in which the reference material is produced and the tests necessary to characterize the material are the decision of the applicant based on the end use of the material. The applicant may consider NIST as a potential subcontractor for measurement and other professional services.

For additional information on this topic, please contact:

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Bioengineering and Genomic Applications, SRG
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National Center on Sleep Disorders Research

The National Center on Sleep Disorders Research (NCSDR) was established within the National Heart, Lung, and Blood Institute (NHLBI) as a result of the National Institutes of Health (NIH) Revitalization Act of 1993. Its mandate is to conduct and support research, training, health information dissemination, and other activities with respect to sleep disorders, including biological and circadian rhythm research, basic understanding of sleep, chronobiological and other sleep related research and to coordinate the activities of the Center with similar activities of other Federal agencies, including the other agencies of the National Institutes of Health, and similar activities of other public entities and nonprofit entities.

Three specific types of research are emphasized: basic research using state-of-the-art approaches to elucidate the functions of sleep and the fundamental molecular and cellular processes underlying sleep; patient-oriented research to improve the diagnosis and treatment of sleep disorders; and applied research to evaluate the scope and health consequences of sleepiness and sleep disorders.

Research opportunities of potential interest to small businesses may include, but are not limited to the following examples:

A. Portable instrumentation for diagnostic in-home assessment of sleep disorders especially sleep disordered breathing.

B. Countermeasures for excessive daytime sleepiness, including methods that alter the output of the circadian clock to optimize sleep and wakefulness.

C. New technologies and instrumentation scaled for high-throughput phenotypic characterization of sleep in mice.

D. High volume, inexpensive assays to assess variations in gene expression related to circadian and behavioral state (sleep and wakefulness) related .

E. Improved methods for the diagnosis of sleep disordered breathing in infants, children, and adults.

F. Educational interventions to improve worksite productivity and school performance through the prevention and management of insufficient sleep and poor sleep environment conditions.

G. Portable inexpensive devices for ambulatory assessment of both sleep and physical activity in population-based biomedical research studies.

H. Methods to improve patient compliance with sleep disordered breathing treatments.

I. New pharmacological for the treatment of sleep disorders, especially sleep disordered breathing.

J. Noninvasive imaging technologies to assess neurophysiological and regional brain blood flow changes associated with sleep disorders and other causes of excessive daytime sleepiness.

For additional information on research topics, please see the National Sleep Disorders Research Plan (http://www.nhlbi.nih.gov/health/prof/sleep/res_plan/index.html) and contact:

Mrs. Ann Rothgeb
Division of Lung Diseases
National Heart, Lung, and Blood Institute
6701 Rockledge Drive, Room 10124 (MSC7952)
Bethesda, MD 20892-7952
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Email: ar31t@nih.gov

NATIONAL INSTITUTE ON AGING (NIA)

The NIA supports biomedical, behavioral, and social research and research training on the aging process as well as on the diseases and other special problems and needs of older people. It supports grant research under four established programs: Biology of Aging, Behavioral and Social Research, Neuroscience and Neuropsychology of Aging, and Geriatrics and Clinical Gerontology.

Examples of research topics within the mission of the NIA that may be of interest to small businesses are shown below. These listings illustrate the range of areas that are of interest to the NIA and are not intended to be exhaustive.

For additional information about areas of interest to the NIA, please visit our home page at http://www.nia.nih.gov.

Phase II Competing Renewal Awards

NIA will accept Phase II Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval.

NIA will accept applications for up to two (2) years and up to $750,000 per year in total costs. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Please contact Dr. Michael-David A.R.R. Kerns (see contact information below) before beginning any work on a Competing Renewal application. Potential applicants must obtain approval from NIA before submitting a Competing Renewal application. After obtaining approval from NIA, prospective applicants are requested to submit a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIA SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities. Research and development efforts can be focused on medications to treat, delay the progression of, or prevent age-related cognitive decline, Alzheimer's disease, and other dementias of aging.

1. Studies for preclinical discovery and development of drugs, natural products, or other types of compounds, including pharmacology and toxicology studies, beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development of the drug or natural product.

2. Completion of studies as required by the FDA for an IND application.
3. Human clinical trials/studies to determine a drug's, natural product's, or other type of compound's safety profile, metabolism, and/or efficacy.

For questions relating to Phase II Competing Renewal applications, please contact:

Dr. Michael-David (MD) A.R.R. Kerns
(301) 402-7713, Fax: (301) 402-2945
Email: kernsmd@mail.nih.gov

Behavioral and Social Research

Research on basic and translational social and behavioral research on aging processes and the place of older people in society. The program focuses on how people change with age, on the interrelationships between older people and social institutions (e.g., the family, health-care systems), and on the societal impact of the changing age-composition of the population. Emphasis is placed upon the dynamic interplay between the aging of individuals and their changing social and physical environments. Special emphasis areas are Aging Minds (see *The Aging Mind: Opportunities in Cognitive Research*, http://books.nap.edu/catalog/9783.html); Genetics, Behavior and the Social Environment; Health Disparities; Health, Work and Retirement; Increasing Health Expectancy; and Interventions and Behavior Change. Areas that may be of interest to small businesses include, but are not limited to:

A. Cognitive and human factors interventions on the individual and environment to maintain independence, maintain functioning, increase well being, and prevent disease/disability. Such interventions can include behavioral technologies, environmental modifications and redesign, training and teaching efforts, or new programs, products and services. Interventions can be developed for home, community, health-care or work-place settings.

B. Research Innovation: Innovations and new products that improve data collection, data analysis, and data dissemination are encouraged. Examples of areas of interest in data collection include, but are not limited to: experience sampling methodologies; improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research; the development of miniaturization devices to improve real-time data collection, and the development of computer-assisted personal and telephone instrument modules to use with older respondents. New and innovative methods for improving the measurement of well-being in the older populations (both across subgroups and internationally), are particularly encouraged.

C. Social, behavioral, environmental and/or technical interventions on the individual for health maintenance and disease/disability prevention. Such interventions can include self management of chronic diseases including behavioral change technologies, enhancing compliance, especially for less educated patients with chronic diseases requiring strict adherence to complex regimens, or new programs, products and services to increase the health, functioning and well-being of older people. Interventions can be developed for home, community, health-care or work-place settings.

D. AIDS and aging. The development of intervention strategies which are designed to prevent the spread of AIDS in middle-aged and older populations. These strategies may include health education programs to inform the health care providers and public about risks of AIDS in older people.

E. Multi-Level Interventions are interventions that influence multiple levels. Levels include the social, community, family, institutional, and individual. More information about the use of multilevel methodology in the social sciences can be found in People and Pixels: Linking Remote Sensing and Social Science (http://books.nap.edu/openbook/0309064082/html/index.html). Other valuable information about social science interventions can be obtained from New Horizons in Health an Integrative Approach (http://books.nap.edu/openbook/0309072964/html/index.html). Interventions and technologies that address multiple levels are of particular interest to the Behavior and Social Research Program.

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F. Interventions for care provision. Development of strategies for care providers (both professionals and families) to deal with burdens

of care associated with chronic disabling illness or disease (including Alzheimer's disease). Interventions include new forms of adult day care, and family interventions. Development of work site programs to supply information on caregiving (including community respite and daycare facilities) and to enable advance planning by employees.

G. Death and dying. Programs that deal with decreasing the trauma and difficulty of elders, their families, and care providers faced with end-of-life decisions and those events that surround the end of life.

H. Long-term adherence. Development of strategies and technologies to enhance long-term adherence to medical regimes for chronic conditions and behavior-change interventions for health promotion in older adults. Adherence advances might target the healthcare provider, caregiver or patient, or a larger group, such as a social network.

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I. Forecasting. Development of mathematical, economic, demographic and epidemiological models that will lead to improved forecasting of national, state and county level estimates of the demand for aging-related services and improved prediction of the effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. For example, micro- and macro-simulation models of changes in health and economic status and methodological enhancements to existing models that takes into account health, intergenerational transfers, changes in family composition, and other characteristics of future cohorts. The program is interested in both domestic and international projections.

J. Measurement instruments and database support. The program supports collection of numerous large datasets and is therefore interested in technologies which lead to products that will facilitate distribution of data while ensuring the confidentiality of NIA supported longitudinal studies are of particular interest. Information on supported datasets can be found at: http://www.nia.nih.gov/research/extramural/behavior/datasets.pdf.

1. Development of new instruments using existing demographic and economic data and theory that yield defensible estimates of quality of health plans, hospitals, nursing homes, etc. The program is interested in both domestic and international estimates.

2. Development of improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research.

3. Development of new technologies which improve large scale longitudinal surveys in the US and abroad. Including the development of computer-assisted personal and telephone instrument modules, including expert systems, to use with older respondents, in order to determine information such as occupational status, migration, housing issues, disability status, and family structure.

4. Development of new databases (e.g., from administrative data) and database support to satisfy data and research needs on aging, and innovative data archives and methods for accessing archives to make current statistical and epidemiological data more accessible to researchers.

5. Development of innovative methods and software to provide improved high performance remote analytic access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality and the need to prevent re-identification of subjects or respondents. Such software would increase the ease with which data analysts could perform sophisticated analyses with a wide range of statistical software programs, while automatically preventing any analyses or remote requests that could compromise data security.

6. The development of high quality micro or macro simulations models that measure the impact of interventions on health expenditures, well-being and other outcomes.

K. Dissemination and teaching materials. Development of innovative teaching and dissemination tools (e.g., dataset-based computer programs, simulations/games, videotapes and other heuristic devices) to

teach dynamics of population aging and convey results of aging research. For example, teaching modules for secondary data analysis for high school and college students using, for example, data from the US Census Bureau, the National Center for Health Statistics, or an NIA sponsored study (see NIA website http://www.nia.nih.gov/research/extramural/behavior/datasets.pdf for available data sets) and projection data.

L. Interventions on the health-care system. Development and evaluation of strategies to improve health-care organization and delivery including attention to assisted living and new forms of in-home care.

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M. Development of indicators and measures of progress in the behavioral and social sciences, including bibliometric measures of citations and impact of research, measures of the rate of change and the formation of new research areas, and measures of the impact of behavioral and social research on public policy and well-being.

Dr. Richard Suzman
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N. Development of miniaturized devices to be used in behavioral and social research to improve real-time, remote monitoring, virtual data collection for instant, continuous, and/or interactive feedback system, and reliable data storage/retrieval.

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Biology of Aging

Research on the physiology, molecular, and cellular basis of aging processes. NIA also has responsibility for maintaining existing resources and developing new resources for aging research, such as populations of well-characterized animals and specific cell lines, for example, human fetal lung fibroblasts. Areas that may be of interest to small businesses include, but are not limited to:

A. Effects of metabolism on the aging process, e.g., how metabolic regulation influences longevity, and the development of anti-oxidant interventions to reduce oxidative stress in vivo.

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B. Development of minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in young and old animals, or development of non-invasive research and test methods for use in animals.

Dr. Nancy Nadon
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Email: nn37a@nih.gov

C. Development of molecular probes such as antibodies, DNA sequences and expression vectors useful in studying aging, senescence, and longevity both in vivo and in vitro.

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or

Dr. Rebecca Fuldner
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Email: Fuldnerr@mail.nih.gov

D. Instruments and/or methodology to monitor dynamic progression of ovarian follicles from primordial through antral stages in humans and other mammals with sufficient sensitivity to obtain an accurate profile during the perimenopausal period when relatively small numbers of follicles are present.

Dr. Frank Bellino
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E. Development of new animal models, including transgenic animals, for studying aging processes, as well as development of new biological model systems for research on aging to replace or reduce vertebrate animal use in research. These models may include better in vitro systems, improved cell culture methods, mathematical models, and computer simulations.

Dr. Nancy Nadon
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F. Development of interventions to slow down the degenerative processes associated with aging. These would include techniques with commercial potential to: (1) manipulate the control of cell proliferation or programmed cell death, (2) reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, (3) improve the damage surveillance and repair potential of cells, (4) improve the immune response to foreign molecules or reduce the response to self, and (5) reverse age-related changes in hormone production and function.

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G. Development of treatments for wound healing in the aged.

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Email: carringtonj@nia.nih.gov

H. Development of appropriate animal and human culture model systems to explore underlying molecular and cellular mechanisms of prostate growth in middle-aged and older subjects.

I. Development of appropriate animal model systems to explore underlying molecular and cellular model systems of female reproductive aging processes as well as the development of pathophysiologic processes associated with the human menopause, including bone loss, cardiovascular pathology, hot flashes, and excessive uterine bleeding.

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Neuroscience and Neuropsychology of Aging

Research on age-related changes in the brain or nervous system in the context of other age-related physiological or homeostatic regulator changes (e.g., endocrine, dietary, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, perceptual and cognitive processes and changes that occur with aging as related to their underlying biological mechanisms. An important component of this program is the support of studies on Alzheimer's disease and related dementias of aging. Areas that may be of interest to small businesses include, but are not limited to:

A. Devices or intervention strategies that may prolong independence when there are dysfunctions of the central nervous system.

B. Development of sensitive, specific and standardized tests for diagnostic screening of cognitive decline and dementia, for example, the development of biochemical and neuroimaging criteria for the diagnosis of cognitive decline and Alzheimer's disease.

C. Discovery, development and/or evaluation of drugs, delivery systems, or treatments to enhance cognitive functioning in normal aging and to treat the cognitive deterioration and/or behavioral symptoms associated with Alzheimer's disease as well as to slow and/or reverse the course of the disease, or prevent it entirely.

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Email: nb12s@nih.gov

D. Nutritional interventions to restore brain biochemical changes in aging and neurodegenerative diseases.

E. Biosensors and prosthetic devices to aid sensory and memory dysfunctions.

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F. New technologies to screen for the presence of sleep disorders in older persons, to aid in the diagnosis of these disorders, and to enable their remediation.

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G. Improved instrumentation, imaging technology, related devices, and software packages for use in visualizing neural activity during cognitive or sensory behavior in older adults. Also of interest would be new technologies to combine neural imaging and behavioral assessment in awake unanesthetized animals.

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H. Development of technology and analysis tools to examine cellular patterns of gene and protein expression in the normal and diseased aging nervous system, including the identification of aberrant gene products expressed in the aging brain. Development of molecular imaging technology for the in vitro and in vivo analysis of gene and protein function in the normal aging brain and in the diseased aging nervous system.

I. Development of technology such as non-invasive methods, to identify neural stem cells and to monitor their function in the adult and aged nervous system Development of novel markers of stem cell proliferation, migration, and differentiation, as well as methods to assess the integration and function of stem cells in the nervous system.

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Dr. D. Stephen Snyder (Alzheimer's disease and other dementias of aging)
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Geriatrics and Clinical Gerontology

The Geriatrics and Clinical Gerontology (GCG) Program supports research on health and disease in the aged and research on aging over the human life span and its relationships to health outcomes. Research on Geriatrics focuses primarily on health issues regarding the aged, and deals with research on disease and disability in older persons, including both specific conditions and issues related to multiple morbidity. Clinical Gerontology Research focuses primarily on clinically related issues regarding aging, and deals with research on aging changes over the life span. A major focus is on the determinants of rates of progression of age-related changes that affect disease risk, particularly those affecting risk for multiple age-related conditions.

Areas of interest include but are not limited to:

A. Research on better ways to prevent injuries and deaths associated with the use of currently available bed rails in older patients; this will include improved designs of bed systems for use in the home, nursing home and hospital.

B. Development of vaccines and other agents for preventing and treating infections in older persons, including development of new vaccines or preventive interventions, and new methods using currently available vaccines or preventive medications.

C. Techniques for preventing or treating urinary incontinence.

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D. Refinements in techniques for the measurement of age-related changes in hormone levels, status or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function). The objective is to enhance sensitivity and achieve greater economy in the assay cost.

E. Effects of menopause on woman's aging and subsequent health. Effects of age-related changes in endocrine status in men on subsequent aging, morbidity and mortality.

1. Refinements in techniques for the measurement of age-related changes in hormone levels or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function).

2 Development and testing of alternative strategies (to conventional estrogen/ progestin therapy) for the management of short-term menopausal symptoms and for the reduction in risks of cardiovascular disease, osteoporosis, and other menopause-related conditions, disorders and diseases. Development and testing of new tissue-specific modulators of estrogen/ androgen receptor activity in men and in women for the prevention or treatment of age-related diseases.

3. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy of

treatment or enhanced risk or progression of adverse effects/events.

4. Determine drug interactions, i.e., potential alterations in pharmacokinetics and pharmacodynamic properties of drugs taken concomitantly with postmenopausal hormones.

F. Osteoporosis. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy, response to treatment or enhanced risk or progression of adverse effects/events.

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Email: ss80t@nih.gov

G. Improved instrumentation (e.g., accelerometers) for assessment of physical activity, and improved monitors for visually and/or biomechanically characterizing falls in older patients.

H. Improved instrumentation and imaging techniques for measuring body composition and properties such as muscle function in older persons.

I. Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).

J. Development of techniques/devices (e.g., non-invasive, portable) for improved monitoring of caloric intake and/or energy expenditure in epidemiological studies.

K. Measurement of deficits in muscle strength and balance among older persons.

1. Instrumentation for biomechanical assessment of ambulation and falls.
2. Quantitative methods of assessing postural perturbations relevant to activities of daily living.

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L. Techniques and methods for screening, diagnosis, and treatment of cancer in older persons.

1. Development of geriatric assessment instruments and/or methodology to assist oncologists in patient evaluation and diagnostic work-up to determine the older patient's overall physical and physiologic health status.
2. Techniques to promote effective pain management in older-aged cancer patients. This includes documentation and assessment of pain intensity and its characteristics prior to and after pharmacologic and non-pharmacologic interventions.
3. Development of innovative teaching tools for physicians, nurses, and other health professionals in the following areas: (1) to convey benefits of screening and early detection of cancer for use with older-aged persons; (2) to assist in teaching older-aged patients in self-examination for early warning signs of cancer; and (3) to teach older aged patients how to care for themselves after cancer surgery (e.g., ostomy patients).
4. Development of methods to be used as guidance for physicians to estimate proper medication dosage in elderly cancer patients given body composition, size, age, other health problems, kidney functioning, and other physiologic parameters. This includes estimates of an initial or loading dose of therapeutic drugs and daily maintenance for continuance of therapeutic concentration of drugs in the patient's bloodstream.

Dr. Rosemary Yancik
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M. Development of devices and techniques for screening substantial numbers of individuals for particular alleles at loci of relevance to human genetic studies of aging.

N. Development and validation of imaging and sensor technologies to improve measures of physiologic changes with age.

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Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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For administrative and budget management questions, contact:

Ms. Linda Whipp
Grants Management Officer
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NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. The NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

For additional information about areas of interest to the NIAAA, you are invited to visit our home page at http://www.niaaa.nih.gov.

Phase II Competing Renewal Awards

NIAAA will accept Phase II SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

You are strongly encouraged to contact Dr. Karen Peterson (contact information provided below) before beginning the process of putting a Phase II Competing Renewal application together. Prospective applicants are also strongly encouraged to submit to Dr. Peterson a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIAAA SBIR/STTR Phase II awards will be eligible for a competing renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II competing renewal projects.

These examples are meant for illustrative purposes and are not exclusive of other appropriate activities:

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants. Some in vivo or in vitro studies would be expected to have been carried out in Phase I or the initial Phase II grant.
- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.
- Development and clinical evaluation of new alcohol-sensitive biomarkers.

- Assessment of devices with regard to performance standards related to the FDA approval process.
- Safety and effectiveness studies of novel medical devices.
- Biocompatibility studies of surface materials of putative medical implants.
- Evaluation of novel imaging approaches for diagnostic purposes.
- Clinical studies in support of New Drug Application approval by the FDA.
- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Direct your questions about scientific/research issues to:

Joanne B. Fertig, Ph.D.
Telephone: (301) 443-0635
Fax: (301) 443-8774
Email: jf75t@nih.gov

Peter B. Silverman, Ph.D.
Telephone: (301) 402-6966
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Forward Letter of Intent to:

Karen P. Peterson, Ph.D.
Acting Chief, Research Policy and Special Projects Branch
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Pharmaceutical Development for Alcoholism Treatment

Applied and, where appropriate, clinical research on pharmacologic agents for use in the treatment or medical management of alcoholism, disorders resulting from alcoholism, the improvement and refinement of drugs currently available for therapeutic purposes, or drugs suitable for use in basic research studies on alcohol addiction. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of agents to attenuate drinking behavior, e.g., drugs to curb craving.

B. Development of aversive agents such as disulfiram that attenuates drinking behavior.

C. Development of agents to treat acute alcohol withdrawal.

D. Development of agents to treat the protracted withdrawal syndrome.

E. Development of neurotransmitter agonists and antagonists, or drugs that enhance the efficacy of neurotransmission, which are capable of improving or reversing alcohol-induced cognitive impairments.

F. Development of agents to induce sobriety in intoxicated individuals (amethystic agents).

G. Development of agents to diminish drinking by treating associated psychiatric disorders and/or drug abuse.

H. Development of improved methods of drug delivery for the treatment of alcoholism. The systems developed must be capable of maintaining therapeutic drug levels for extended periods of time to alleviate compliance problems.

I. Development of drugs for the treatment of alcoholic hepatitis, cirrhosis, pancreatitis, and cardiomyopathy.

J. Research on the pharmacokinetics of concurrent ethanol and other drug use.

For clinical questions, contact:

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For pre-clinical questions, contact:

Mark Egli, Ph.D.
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Diagnostic Assessment of Alcohol Use Disorders and Comorbidity

Innovative self-report and biochemical approaches to the early identification of alcohol use problems and diagnosis of alcohol use disorders and comorbidity are needed. The research design should include measurements of reliability and validity in appropriate population samples. Areas that may be

of interest to small businesses include, but are not limited to:

A. Development or adaptation of diagnostic instruments measuring alcohol use disorders and related comorbid conditions in general population and treated samples, including youth, the elderly, pregnant women, ethnic minorities, the handicapped, and persons with low-level reading skills).

B. Development and testing of methodology to translate diagnostic instruments for alcohol use disorders and associated disabilities into relevant different languages (e.g., various Hispanic languages).

C. Development and testing of computer algorithms necessary to derive diagnoses of alcohol use disorders and associated comorbidity.

D. Development of computer software for utilization of assessment instruments in a clinical setting. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.

E. Application of statistical and mathematical analyses to develop models designed to increase our understanding of (1) etiologic relationship between alcohol use disorders and their associated disabilities, and (2) the factors that influence the initiation and maintenance of alcohol use disorders.

F. Identification, validation, and assay of physiological and/or biochemical measures capable of identifying individuals at risk for becoming alcoholics or individuals who already exhibit alcohol problems. The accurate measurement of acetaldehyde conjugates or abnormal glycoconjugates in blood is one promising approach.

G. Development of biochemical/physiological methods for early detection of alcohol-derived pathology, e.g., alcoholic hepatitis or cirrhosis. Development and characterization of markers to accurately predict vulnerability to alcohol-derived pathology.

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(301) 443-0637
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Treatment of Alcoholism

A. Development and evaluation of innovative treatment approaches. These approaches can include outreach, shelter, detoxification, treatment and recovery, and alcohol-free housing, as appropriate.

B. Development and validation of tools to aid in the clinical management of patients, including selection of appropriate interventions, process evaluation, assessment of outcome, aftercare, and patient tracking, in various treatment settings.

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Measurement of Alcohol Consumption/Impairment

Development of new methods for quantitative measurement of alcohol consumption, development of new and more accurate cost-effective technological approaches for non-invasive measurement of blood alcohol concentration, and development of novel approaches to measure and quantify alcohol-induced impairment of human performance. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of new methods for quantitatively estimating alcohol use over a period of days or weeks. The approaches should have high sensitivity and specificity and have utility in a variety of settings, including treatment compliance monitoring. Integration of measurement devices with electronic devices to transmit and/or record data in real time is desirable.

B. Development of new and more accurate cost-effective technological approaches (such as breathalyzers) for non-invasive measurement of blood alcohol concentration in law enforcement, workplace, research, and clinical settings.

C. Development of instruments involving tests of behavioral, cognitive, and/or motor function to measure and quantify alcohol-induced impairment of human performance. Such instruments may be computer-based and may be designed to simulate specific work situations such as driving performance, use of complex machinery, learning and retention of new information.

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Promoting Adherence to Medical, Pharmacologic, and Behavioral Treatments

Several recent reports and literature reviews point to the continuing need for improving adherence to therapeutic regimens. Adherence rates vary considerably across diseases and treatments, measuring instruments, and populations, with rates ranging from 30% to 60% in many instances. The reasons for non-adherence are multifaceted. Health-care providers, organizational systems, and patient factors all play a role in adherence to therapeutic regimens. Thus, to understand and eventually improve adherence, conceptual frameworks and interventions need to take into account institutional, system, situational, interpersonal, and personal factors as well as the characteristics of the illness or condition and of the treatment regimen. While extensive research exists and successful techniques have been identified, greater efforts are needed to develop and implement programs based upon these findings. Applications are sought to develop:

A. Programs to implement effective interventions and to evaluate their implementation.

B. Professional education courses or web-based training modules on interventions and to monitor their effectiveness.

In both cases, the emphasis is on how to encourage health practitioners to utilize interventions that will improve their patients' adherence to medical, pharmacologic, and behavioral regimens for alcohol abuse and dependence.

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Prevention

Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Applicants are strongly encouraged to consult with research methodologists and statisticians to ensure that state-of-the-art approaches to design, analysis, and interpretation of studies under this topic are used. Areas that may be of interest to small businesses include, but are not limited to:

A. Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Special emphasis should be placed on the needs of high-risk groups, ethnic and minority populations, youth, children of alcoholics, women, the handicapped, and the elderly. Examples of such materials include school-based curricula, interactive videos, computer-based multimedia programs, training manuals for teachers or parents, and community-based programs.

B. Development and evaluation of educational materials designed to inform the elderly about specific age-related risks for alcohol problems. Particular attention should be given to age-related reductions in alcohol tolerance, interactions between alcohol and prescription and over-the-counter medications, possible exacerbation of some medical conditions common among the elderly, potential biomedical and behavioral consequences of excessive alcohol use, and the role of alcohol in falls, fires, burns, pedestrian and traffic injuries, and other unintentional injuries.

C. Development and evaluation of educational materials designed to provide information on date rape, spouse abuse, child abuse, and other types of violence that have been found to be associated with alcohol use and/or abuse. The development of strategies for preventing victimization would also be appropriate.

D. Development of instruments and educational materials designed to improve the effectiveness of employee assistance programs, especially with respect to assessment, referral, and health promotion as it relates to alcohol use and abuse.

E. Development and evaluation of statistical analysis programs tailored to the design and analysis of alcohol prevention-relevant research. Programs could focus on a variety of areas including: imputation of missing data under varying design assumptions; simulation of distributions of outcomes based on varying mixtures of sample populations; application of chronic or infectious disease models to targeted communities; and models of the

potential effect of various policy-based interventions, such as increased taxation or reduction of outlet density by license revocation and control.

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Health Services Research on Alcohol-Related Problems

Research projects are sought that will expand knowledge and improve delivery of alcohol treatment and prevention services. The research objectives include, but are not limited to: the effects of organizational structures and financing mechanisms on the availability, accessibility, utilization, delivery, content, quality, outcomes, and costs of alcohol treatment services. Objectives also include studying the effectiveness and cost-effectiveness of alcohol prevention services in reducing the demand for health care services and improving the methodological tools useful for conducting health services research. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of computer software or other protocols to assist in the management of treatment delivery. Software should be useful for assessment, diagnosis, patient placement criteria, monitoring of services received, tracking patient progress, and billing.

B. Development of software or other protocols to assist clinicians in scoring and norming results of commonly used assessment instruments. Output should be in a form useful for guiding client feedback.

C. Development of software or other protocols to assist treatment programs and service agencies in measuring, assessing, or otherwise documenting indicators of clinical performance or improvements in quality of service provision.

D. Development of products to facilitate the adoption of evidence-based research findings into everyday clinical practice. For example, training videos or other materials illustrating research-based improvements in treatment practice could provide clinicians with practical examples of orienting patients to pharmacotherapy, assessing motivational readiness, giving motivational feedback, establishing contracts for behavioral couple therapy, and conducting brief interventions in primary care settings.

E. Development of software or other protocols to facilitate the incorporation of screening and identification tools into routine usage in primary care, emergency, obstetric, mental health, and other health care settings. Research projects should facilitate both the provisions of brief interventions and effective referral to specialized alcohol treatment.

F. Development of software or other protocols for monitoring clinical costs of alcohol treatment services. These tools should provide a user-friendly system of monitoring costs that could be implemented without additional accounting expertise by the staff at a typical treatment setting. At the same time, such tools should be defensible as measures of the true opportunity costs of providing alcohol treatment services. Such software might be bundled with billing software.

Robert Huebner, Ph.D.
(301) 443-4344
Email: bhuebner@mail.nih.gov

Training in Alcoholism Assessment and Treatment Techniques

Development of educational materials, including computer-based approaches, for training of health professionals in the use of various assessment techniques and treatment strategies. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of educational materials, including computer-based approaches, for training of health professionals and paraprofessionals in the use of various assessment techniques and instruments.

B. Development and evaluation of clinical protocols which enable health professionals to relate assessment to appropriate intervention and treatment strategies.

C. Development and evaluation of effective health professions training programs which utilize state-of-the-art educational technology and are based upon currently accepted clinical and behavioral strategies. Examples include experiential teaching technologies such as standardized patient, interactive video, and computer simulation.

Jason Lazarow, M.Ed.
(301) 435-8043
Email: jlazarow@mail.nih.gov

Fetal Alcohol Syndrome (FAS) and Alcohol-Related Birth Defects

FAS is a severe developmental disorder that includes mental retardation, cognitive and behavioral disabilities, and motor impairment. The NIAAA supports research leading to improved diagnosis and assessment of impairment and disability, as well as the development of tools to enhance academic and daily living skills. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of diagnostic and/or screening methods that can be used prenatally to identify fetuses affected by ethanol.

B. Development and validation of assessment methods to provide more accurate clinical diagnosis of FAS at all life stages.

C. Development and testing of skill-building, therapeutic, and education program products that enhance the social, cognitive, adaptive and motor abilities of individuals with FAS or fetal alcohol effects.

D. Development of accurate measures of the responsiveness of children affected by prenatal exposure to alcohol to stress and predictors of vulnerability to alcohol-drinking or other psychopathology during adolescence and adulthood.

E. Development and evaluation of educational and training programs designed to enhance the skills of non-professional caregivers in dealing with the problems associated with FAS.

For clinical research questions, contact:

Deidra Roach, M.D.
(301) 443-5820
Email: droach@mail.nih.gov

For prevention research questions, contact:

Marcia Scott, Ph.D.
(301) 402-6328
Email: mscott@mail.nih.gov

For basic research questions, contact:

Laurie Foudin, Ph.D.
(301) 443-0912
Email: lf29z@nih.gov

Science Education

The NIAAA Science Education program is intended to: (1) supplement in-service education of health professionals and paraprofessionals with respect to their recognition and treatment of alcohol-related medical problems; (2) stimulate the interest of both precollege and college students, especially among underserved populations, in career opportunities in the biomedical and behavioral sciences generally and the alcohol field specifically; (3) enhance precollege education in the classroom, both directly and via support to teachers, in the life sciences and in education regarding science-related personal and societal challenges; and (4) improve public understanding of science generally and with particular regard to the role of and need for alcohol research. The NIAAA Science Education program complements, but does not duplicate, the education and training components described under other NIAAA topics.

Efforts in science education might include, but are not limited to:

A. Development of methodology to transfer new alcohol research knowledge and directions of scientific knowledge growth to curriculum developers and science teachers, consistent with the National Research Council's National Science Education Standards (1996).

B. Development and testing of specific science education materials, activities or programs to implement one (or more) of the four stated objectives of the NIAAA science education program. The creative use of emerging educational and telecommunications technologies in this regard is of special interest.

C. Development and testing of methodology to present science and alcohol abuse-related curricula and educational materials to particular underserved group(s) in culturally relevant ways, and/or to obtain community support for education in science-related and alcohol-related topics that may be culturally sensitive.

D. Development of resource materials on scientific career opportunities in fields of interest to NIAAA, reflecting activities (e.g., focus groups) and research on motivational factors influencing high school students' career choices, and reflecting economic and social projections of career outlooks for the 21st century.

Jason Lazarow, M.Ed.

(301) 435-8043
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Longitudinal Analysis of Complex Survey Data

Despite recent advances made in developing software programs for longitudinal latent and observed variable structural modeling, very little has been accomplished in this research arena regarding modeling with complex sample data. Currently there is no comprehensive statistical software package that allows such modeling that takes into account sampling weights, stratification and clustering while at the same time allowing for these observed variables to be either categorical, continuous, or a combination of both. Moreover, there is no currently available comprehensive statistical package that allows for the longitudinal analysis of complex survey data for the variety of models necessary for the analysis of alcohol-related longitudinal data (e.g., linear, probit and logistic regression, survival analysis [continuous and discrete-time allowing for time-varying covariates], path analysis, exploratory and confirmatory factor analysis, growth modeling, growth mixture modeling, multilevel modeling, linear and nonlinear growth modeling, and combinations and variants of these models).

Bridget Grant, Ph.D.
(301) 443-7370
Email: bgrant@willco.niaaa.nih.gov

Research Tools

The NIAAA supports basic and applied research to develop new or improved tools to enhance laboratory studies on humans and animals. Examples include transgenic animal models, cell lines, new ligands for neuroimaging, and simulators of alcohol impairment. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of animal models, including transgenic animals, possessing specific traits of significance for the study of alcoholism, or for the study of specific pathologic disease states which arise from excessive alcohol consumption.

B. Development of a hepatocyte cell line capable of maintaining viability and metabolic functions in culture systems for an indefinite period.

C. Development of new methods of ethanol administration to animals that produce precise dose control.

D. Development of specialized cell culture chambers to provide controlled administration of ethanol to in vitro cell systems.

E. Development of ligands for alcohol-relevant neurotransmitter systems which will enhance the potential usefulness of PET and SPECT imaging technologies for the study of the etiology of alcoholism and related brain pathology.

F. Development of instruments that simulate driving, piloting aircraft, or using other complex machinery under hypothetical or actual drinking handicaps and are designed to predict fatal and nonfatal accident involvement.

Laurie Foudin, Ph.D.
(301) 443-0912
Email: lf29z@nih.gov

Development and Clinical Testing of Biochemical Markers

The development of effective biochemical markers represents a powerful means for early diagnosis and treatment of alcohol dependent/abuse patients and for the identification of individuals who have a predisposition for alcoholism. There are two different types of biochemical markers: trait markers and state markers.

Trait biomarkers have the ability to detect inborn characteristics of individuals who are vulnerable for alcoholism. This type of marker would be invaluable for screening of high-risk individuals (e.g., children of alcoholics) and targeting them with preventive or early treatment interventions. In addition, trait markers might assist practitioners in identifying subpopulations of alcoholics who may need different treatment strategies. An ideal trait marker should have several features. First, it should display validity in detecting people susceptible to alcoholism, particularly before the onset of alcoholism or during periods of stable abstinence. Second, it should be easily and reliably measured. Third, it should be specific for alcoholism only and not affected by other medical or psychiatric disorders or drugs. Since alcoholism is a complex disease, it is likely that more than one type of gene and protein exist as trait marker.

State markers or markers of alcohol consumption serve several important purposes. First, they can assist physicians in diagnosing individuals with chronic drinking problems, particularly patients who deny excessive drinking. Moreover, they may also

identify individuals in early stages of heavy drinking, thus avoiding the long-term medical, psychological, and social consequences of chronic alcoholism. Second, state biomarkers can aid in the diagnosis and treatment of other diseases (liver diseases, pancreatitis, and cardiovascular diseases) that were, at least, caused by excessive drinking. Third, they are useful in alcohol treatment and prevention programs. Since the goal of many of programs is abstinence, monitoring relapse is important in gauging success. Last, state biomarkers are important in clinical alcohol trials. Although self-reports have become more sophisticated and valid (e.g., Timeline Followback), they still rely on accurate reporting. These new and reliable biomarkers could then be used to confirm the self-report. Several biomarkers with certain limitations are currently in use including carbohydrate-deficient transferrin (CDT), gamma glutamy transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and mean corpuscular volume (MCV). New state markers need to be developed that incorporate the following attributes: validity, reliability, stability, cost, practicability, acceptability, and transportability.

Areas that may be of interest to small businesses include, but are not limited to:

A. Develop and evaluate clinically alcohol-sensitive biomarkers to identify individuals who are predisposed to alcoholism; determine relapse; measure levels of drinking; and determine alcohol-induced tissue damage.

B. Identify genes, and proteins that are expressed during the development of alcohol dependence for biomarker development.

C. Develop methodologies for high throughput identification of alcohol metabolites and other signaling molecules that are expressed during alcohol intake.

D. Use knowledge of genetic and molecular mechanisms underlying alcohol-induced organ damage (including alcohol-related liver, pancreas, heart disease and FAS) to develop new biomarkers of tissue and cell damage.

E. Evaluate clinically innovative alcohol-sensitive biomarkers (trait, relapse, organ damage) for sensitivity and specificity.

For clinical questions contact:

Raye Z. Litten, Ph.D.
(301) 443-0636

Email: rlitten@niaaa.nih.gov

For pre-clinical questions, contact:

Denise A. Russo, Ph.D.
(301) 402-9403

Email: drusso@mail.nih.gov

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Karen P. Peterson, Ph.D.
Acting Chief, Research Policy and Special Projects Branch
Office of Scientific Affairs
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane
Bethesda, MD 20892
For Federal Express delivery, use:
Rockville, MD 20852-1705
Phone: (301) 451-3883, Fax: (301) 443-6077
Email: kpeterso@mail.nih.gov

For administrative and business management questions, contact:

Ms. Judy Fox
Grants Management Officer
National Institute on Alcohol Abuse and Alcoholism
Phone: (301) 443-4704, Fax: (301) 443-3891
Email: js182a@nih.gov

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

The NIAID's Division of AIDS, Division of Allergy, Immunology, and Transplantation, and Division of Microbiology and Infectious Diseases fund SBIR/STTR grants on topics related to their mission and activities as described below. Questions on specific research areas may be addressed to the NIAID Program Officials listed below. General questions on the NIAID SBIR and STTR programs and on administrative and business management may be addressed to contacts listed for the NIAID section. When possible, *applicants are encouraged to use email* for communication.

For information about NIAID's Small Business High-Priority Areas of Interest, please visit http://www.niaid.nih.gov/ncn/sbir/sbirareas.htm.

Phase II Competing Renewal Awards

The NIAID will accept Phase II SBIR/STTR Competing Renewal SBIR/STTR grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA). Projects that are particularly encouraged include those in the NIAID Small Business High Priority Areas of Interest (http://www.niaid.nih.gov/ncn/sbir/sbirareas.htm) and also:

- therapeutics (drugs or antibodies) to treat HIV infections
- therapeutics (drugs or antibodies) for HIV-related opportunistic infections
- anti-inflammatory therapeutics
- transgenic transplantation strategies
- new or improved vaccines, antiviral or antimicrobial agents for infectious diseases

NIAID will accept Phase II Competing Renewal applications for a project period of up to three years and a budget not to exceed a total cost of $1 million per year (including direct cost, F&A, and fee/profit) provided the time period and amount are well justified.

The total amount of all consultant costs and contractual costs normally may not exceed 50% of the total costs requested for initial SBIR Phase II applications. SBIR Phase II Competing Renewal grant applications may exceed this guideline, however, when well justified and when those costs are necessary to support clinical studies or trials and related expenses. Examples of well founded reasons for exceeding this guideline include, but are not limited to, subcontracts for safety, toxicity, or efficacy testing in animals, subcontracts to clinical research organizations to carry out aspects of clinical evaluation or subcontracts to assure compliance with Good Manufacturing Practices expectations of the FDA.

Human clinical trials may not be a component of the proposed research. As announced in Notice NOT-AI-05-021 (http://grants.nih.gov/grants/guide/notice-files/NOT-AI-05-021.html) NIAID will only support investigator-initiated clinical trials through a two part grant process: (1) a clinical trial planning grant followed by (2) a clinical trial implementation cooperative agreement.

NIAID does NOT request a letter of intent. However, prior to submission of a Competing Renewal application, applicants are strongly encouraged to contact:

Gregory Milman, Ph.D.
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room 2153, MSC-7610
6700-B Rockledge Drive
Bethesda, MD 20892-7610 (US Mail)
Rockville, MD 20817-7610 (Delivery Services)
Telephone (301) 496-8666
Fax: (301) 402-0369
Email: gm16s@nih.gov

Division of AIDS

The Division of AIDS (DAIDS) supports research on the pathogenesis, natural history, and transmission of HIV and HIV disease, and promotes progress in its detection, treatment, and prevention.

Director: Dr. Ed Tramont
(301) 496-0545
Email: et89f@nih.gov

BIOSTATISTICS RESEARCH BRANCH

Statistical methods in HIV studies.

Dr: Misrak Gezmu
(301) 435-3722
Email: mgezmu@niaid.nih.gov

BASIC SCIENCES PROGRAM

Supports basic and applied research on the causes, diagnosis, treatment and prevention of HIV and AIDS.

Director: Dr. Carl Dieffenbach
(301) 496-9112
Email: cdd@nih.gov

A. ***Epidemiology Branch.*** Population-based research of HIV transmission and associated biological, behavioral, and environmental factors including correlation between immunologic and virologic events and clinical outcome trends in natural history; correlation between immunologic and virologic events and clinical outcome; and trends in natural history.

Contact: Joana Roe
(301) 435-3759
Email: jr108r@nih.gov

B. ***Pathogenesis Branch.*** Molecular and cellular biology, virology, and immunology of virus-host interactions and mechanisms of immunopathogenesis and HIV transmission.

Contact: Ann Namkung, M.P.H.
(301) 496-9176
Email: an107z@nih.gov

C. ***Targeted Interventions Branch.*** Research areas: (1) targeted therapeutics emphasizing under-explored viral and cellular targets; (2) innovative therapeutic strategies including immune-based and gene-based therapies and therapeutic vaccines; (3) translational research for effective therapeutics spanning preclinical discovery to pilot clinical studies in humans; (4) preclinical discovery and development of topical microbicides and other entities for non-vaccine prevention strategies; and (5) animal models for evaluating new therapeutic entities, regimens, and strategies.

Contact: Dr. Roger Miller
(301) 496-6430
Email: rm42i@nih.gov

VACCINE AND PREVENTION RESEARCH PROGRAM

Supports the development of vaccines and other biomedical and behavioral interventions to prevent AIDS.

Director: Dr. Margaret (Peggy) Johnston
(301) 402-0846
Email: pj7p@nih.gov

A. ***Vaccine Clinical Development Branch.*** Research areas: (1) coordination of phase I, II, and III domestic and international clinical trials of candidate AIDS vaccines; (2) coordination of the characterization of immune responses in HIV-infected and uninfected immunized volunteers; and (3) coordination of studies to identify, validate, and standardize immunologic and virologic markers for monitoring response of participants in vaccine clinical trials.

Acting Chief: Dr. Joseph Chiu
(301) 402-2311
Email: jchiu@niaid.nih.gov

B. ***Prevention Science Branch.*** Conduct of domestic and international phase I, II, and III clinical trials to evaluate HIV/AIDS prevention strategies, including microbicides, chemoprophylactic agents, and other biomedical and behavioral risk reduction interventions. Basic research on mechanisms of sexual and mother-to-child HIV transmission supportive of new biomedical strategies for interrupting transmission. Translational research on microbicides, spanning preclinical through pilot human clinical research. Pilot clinical studies of the performance of microbicide vehicles and applicators with regard to coverage of and persistence on mucosal surfaces as well as behavioral acceptability.

Acting Chief: Dr. Monica Ruiz
(301) 435-8896
Email: mruiz@niaid.nih.gov

C. ***Preclinical Research and Development Branch.*** Support of applied preclinical development of candidate AIDS vaccines, delivery methods, and adjuvants for the prevention of AIDS; promotion and evaluation of safety and efficacy of the prevention modalities, especially novel vaccine concepts identified in preclinical models including trials in non-human primates; genetic and immunologic variation; and mucosal immunity in SIV, HIV, and SHIV models.

Contact: Dr. Yen Li
(301) 496-3816
Email: yl81g@nih.gov

THERAPEUTICS RESEARCH PROGRAM

Develops and oversees research and development of therapies for HIV disease, including complications and co infections, and cancers, in adults, infants, children, and adolescents.

Director: Dr. Sandra Lehrman
(301) 496-8210
Email: slehrman@niaid.nih.gov

A. ***Clinical Research Management Branch.*** Management of grants and contracts supporting therapeutic clinical trials.

Chief: Ms. Margaret Matula
(301) 496-8214
Email: mmatula@niaid.nih.gov

B. ***Drug Development and Clinical Sciences Branch.*** Discovery and preclinical development of experimental therapies for HIV, TB and other infectious diseases; maintenance of a database of potential anti-HIV and -OI compounds; immunologic, virologic, and

pharmacologic research related to the design and conduct of clinical trials.

Contact: Dr. Chuck Litterst
(301) 402-0132
Email: cl30x@nih.gov

C. ***HIV Research Branch.*** Clinical research of strategies to treat adult primary HIV infection and complications; strategies to augment HIV immune responses and general host immunity.

Chief: Dr. Carla Pettinelli
(301) 402-5582
Email: cp22n@nih.gov

D. ***Complications & Co-Infections Research Branch.*** Preclinical and clinical research to develop improved therapies for the treatment and prophylaxis of AIDS-associated opportunistic infections and other complications, including Pneumocystis carinii pneumonia, tuberculosis, Mycobacterium avium disease, hepatitis C, cryptococcosis and Cryptosporidium parvum (the microsporida). Research on metabolic complications of anti-retroviral therapy, emergence of resistance to existing therapies and drug-drug interactions.

Chief: Dr. Barbara Laughon
(301) 402-2304
Email: bl17u@nih.gov

E. ***Pediatric Medicine Branch.*** HIV therapies in children and adolescents, strategies to reduce transmission from mother to infant or fetus.

Contact: Daniella Liynat
(301) 435-3775
Email: DL28a@nih.gov

Division of Allergy, Immunology, and Transplantation

The Division of Allergy, Immunology, and Transplantation (DAIT) supports studies of the immune system in health and the cause, pathogenesis, diagnosis, prevention, and treatment of disease caused by immune dysfunction.

Director: Daniel Rotrosen, M.D.
(301) 496-1886
Email: drotrosen@niaid.nih.gov

A. ***Asthma, Allergy, and Inflammation Branch.*** Asthma, atopic dermatitis, hypersensitivity reactions, rhinitis, sepsis, sinusitis, urticaria, molecular basis of hypersensitivity, basic studies of asthma and allergy mechanisms, new therapies for asthma and allergic diseases, epidemiology and prevention, phagocyte biology, and mechanisms of host defense. Methodologies to design, manage, and analyze clinical and epidemiologic research of the etiology, prevention, and treatment of asthma, allergy, and inflammatory diseases.

Chief: Dr. Charles Hackett
(301) 496-8973, Fax: (301) 402-2571
Email: chackett@niaid.nih.gov

B. ***Basic Immunology Branch.*** Origin, maturation, and interactions of immune cells, immune cell receptors, ligands, cytokine biology, molecular basis of activation, antigen recognition, tolerance, immune response regulation, hematopoiesis and stem cell biology, enhancement of vaccine effectiveness in neonates and adults and basic immunology of vaccines and immunotherapeutics as medical countermeasures for biodefense..

Chief: Dr. Helen Quill
(301) 496-7551, Fax: (301) 402-2571
Email: hquill@niaid.nih.gov

C. ***Clinical Immunology Branch.*** Preclinical and clinical research to develop and improve therapies for the treatment of autoimmune diseases, primary immune deficiencies (not HIV), basic research of disease mechanisms, immunotherapy of disease processes, disorders mediated by lymphocyte products, and mucosal immunity.

Chief: Dr. James McNamara
(301) 451-3121, Fax: (301) 480-1450
Email: jmcnamara@niaid.nih.gov

D. ***Transplantation Immunobiology Branch.*** Acute and chronic graft rejection, allogeneic and xenogeneic transplantation, development of immunomodulatory agents to prevent and treat graft rejection, genomics of the alloimmune response, hematopoietic stem cell transplantation, major histocompatibility complex, minor histocompatibility antigens, infectious and malignant complications of immunosuppression in transplantation, technologies for MHC typing.

Chief: Dr. Shiv Prasad
(301) 496-5598, Fax: (301) 480-0693
Email: sprasad@nih.gov

Division of Microbiology and Infectious Diseases

The Division of Microbiology and Infectious Diseases (DMID) supports research to control diseases caused by all infectious agents, except HIV, through basic investigation of microbial physiology and antigenic structure, pathogenesis, clinical trials of drugs and vaccines, and epidemiologic studies. DMID also supports medical diagnostics research, which is defined as research to improve the quality of patient assessment and care that would result in the implementation of appropriate therapeutic or preventive measures. DMID does not support research directed at decontamination or the development of environmentally oriented detectors, whose primary purpose is the identification of specific agents in the environment. Note that some of the organisms and toxins listed below are considered NIAID priority pathogens or toxins for biodefense research.

Director: Dr. Carole Heilman
(301) 496-1884
Email: ch25v@nih.gov

A. ***Bacteriology and Mycology Branch.***
Bacterial diseases: anthrax and other zoonotic infections (plague, tularemia, brucellosis, leptospirosis, glanders, melliodosis), actinomycete infections, enterococcal infections, legionellosis, Lyme disease, nosocomial infections, rickettsial and related diseases: ehrlichiosis, anaplasmosis, bartonellosis, typhus, Q fever, tickborne spotted fevers, sepsis, staphylococcal infections, urinary tract infections, vector-borne bacterial infections; fungi and fungal diseases: aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, Pneumocystis carinii, other primary and opportunistic fungal infections; antibacterial and antifungal drug resistance; host-pathogen interactions; genetics, molecular, and cell biology; medical bacteriology and mycology; microbial structure and function; development of vaccines, drugs, and medical diagnostics; clinical trials of antibacterial and antifungal agents; and application of proteomics and genomics to facilitate advances in the areas listed above. The Bacteriology and Mycology Branch does not support applications covering environmental detection and decontamination.

Chief: Dr. Dennis M. Dixon
(301) 496-7728, Fax: (301) 402-2508
Email: dd24a@nih.gov

B. ***Enteric and Hepatic Diseases Branch.***
Research areas: (1) diseases and organisms: astrovirus, Bacteroides, Campylobacter, Clostridium including botulinum neurotoxin, commensals, Crohn's Disease, diarrhea, enterotoxins, Escherichia coli, gastroduodenal disease, gastroenteritis, Guillain-Barré, Helicobacter, Listeria, normal flora, Noroviruses including Norwalk, ricin toxin, rotaviruses, Salmonella, Shigella, Staphylococcus, toxins, ulcers, Vibrio, enteric Yersinia, viral hepatitis, hepatitis A, B, C, D, E, G, TTV, SEN-V, animal model hepatitis viruses and newly identified hepatitis viruses; (2) basic virology and bacteriology, genome sequencing, natural history and pathogenesis; (3) immunology of infectious diseases including mechanisms of recovery and persistence, protective immune responses and immunopathogenesis in humans and animal models; (4) vaccine research and development including novel approaches and delivery systems to prevent infection as well as to control and treat disease; (5) development and evaluation of adjuvants and vaccine vectors; (6) identification of new therapeutic targets and development and evaluation of therapeutics; (7) immunotherapy discovery and development; (8) epidemiology, ecology, zoonoses, and transmission; (9) antimicrobial resistance of these organisms in non-nosocomial settings; (10) development of tools for rapid medical diagnosis of organisms, specific targets, disease, and markers of disease outcome; (11) clinical studies and trials; (12) development of model systems to study infection and disease and evaluate vaccines and drugs; and (13) characterization and exploitation of the role of normal flora in disease preventive therapy. Special emphasis areas include development of a single diagnostic to identify multiple diarrheal pathogens, pediatric vaccines to prevent the major causes of worldwide diarrhea, more stable vaccines and formulation improvements, hepatitis C vaccines, novel therapeutics for chronic hepatitis B and C, and improved therapies and vaccines for the botulinum neurotoxins.

Chief: Dr. Leslye Johnson
(301) 496-7051, Fax: (301) 402-1456
Email: lj7m@nih.gov

C. ***Parasitology and International Programs Branch.*** Research areas: (1) protozoal infections, amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis, Helminth infections, cysticercosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes), Invertebrate vectors/ectoparasites, blackflies, mosquitoes, ticks, snails, mites; (2) parasite biology (genetics, genomics, physiology, and biochemistry); (3) protective immunity, immunopathogenesis, evasion of host responses; (4) clinical and epidemiologic studies of the natural history of parasitic diseases; (5) research and development of vaccines, drugs, immunotherapeutics, and medical diagnostics, and (6) vector biology and control; mechanisms of pathogen transmission.

Chief: Dr. Lee Hall
(301) 496-2544, Fax: (301) 402-0659
Email: lhall@niaid.nih.gov

D. ***Respiratory Diseases Branch.*** Research areas: (1) viral respiratory diseases, including those caused by: coronaviruses (including SARS), orthomyxoviruses (including influenza A, B and C), and paramyxoviruses (including parainfluenza viruses and respiratory syncytial virus); (2) bacterial respiratory diseases, including those caused by Moraxella catarrhalis (chronic obstructive pulmonary disease), Pseudomonas aeruginosa and Burkholderia cepacia (associated with cystic fibrosis), Corynebacterium diphtheriae (diphtheria), groups A and B streptococci, Haemophilus influenzae, Neisseria meningitidis, Bordetella pertussis (pertussis), Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae and Klebsiella pneumoniae; (3) Otitis media; (4) mycobacterial diseases, including those caused by: M. tuberculosis (tuberculosis), multi-drug resistant M. tuberculosis, M. leprae (leprosy), and M. ulcerans and other non-tuberculous mycobacterial diseases; (5) development and licensure of vaccines and therapeutic agents for treating and preventing respiratory diseases; (6) maternal immunization; (7) basic research on the pathogenesis, immunity, structural biology, molecular genetics, and genomics of respiratory pathogens; (8) epidemiology and natural history of respiratory pathogens; (9) development of better and more rapid medical diagnostics; and (10) understanding the etiology and long-term health impact of respiratory pathogens in various populations.

Contact: Dr. Gail Jacobs
(301) 496-5305, Fax: (301) 496-8030
Email: gjacobs@niaid.nih.gov

E. ***Sexually Transmitted Infections Branch.*** Development of medical diagnostics, drugs, topical microbicides, and vaccines for sexually transmitted infections (STIs) and other reproductive tract syndromes, such as bacterial vaginosis; molecular immunology; vaginal ecology and immunology; epidemiologic and behavioral research; genomics and proteomics of sexually transmitted pathogens; adolescents and STIs; STIs and medically underserved populations and minority groups; STIs and infertility and adverse outcomes of pregnancy; role of STIs in HIV transmission; role of HIV in altering the natural history of STIs; and other sequellae of STIs.

Contact: Elizabeth Rogers
(301) 451-3742, Fax: (301) 480-3617
Email: erogers@niaid.nih.gov

F. ***Virology Branch.*** Acute viral infections and zoonoses, dengue and other arthropod-borne viral diseases (mosquito-borne encephalitis, including West Nile, yellow fever, etc.), hantaviruses, hemorrhagic fevers (Ebola, Lassa, South African hemorrhagic fevers, etc.), measles, polio, coxsackie virus, and other enteroviruses, poxviruses, rabies, rubella; persisting viral diseases and viruses: adenoviruses, bornaviruses, coronaviruses, herpesviruses, parvoviruses, prion diseases; emergence of viral disease; mechanisms of replication, permissiveness, persistence, and latency; vaccines; immune protection and evasion and viral vectors; epidemiology and viral evolution; structure and function of viruses and viral proteins; molecularly targeted approaches to identify and characterize antiviral targets and agents; chemical design and synthesis of novel antiviral agents; in vitro screening and evaluation of antiviral activity; preclinical therapeutic and some prophylactic evaluations of human viral infections in animal models; clinical trials of vaccines and therapies for viral infections; research of civilian defenses for potential bioterrorist use of viruses; and development of rapid medical diagnostic systems. The Virology Branch does not support

applications covering environmental detection and decontamination.

Chief: Dr. Catherine A. Laughlin
(301) 496-7459, Fax: (301) 402-0659
Email: cl28r@nih.gov

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Dr. Gregory Milman
National Institute of Allergy and Infectious Diseases
(301) 496-8666, Fax: (301) 402-0369
Email: gmilman@niaid.nih.gov

For administrative and business management questions, contact:

Ms. Mary Kirker
Grants Management Officer
National Institute of Allergy and Infectious Diseases
(301) 496-7075, Fax: (301) 480-3780
Email: mk35h@nih.gov

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)

The NIAMS supports research in arthritis and musculoskeletal and skin diseases. Such research is directed at basic understanding of the causes and development of rheumatic diseases, connective tissue diseases, musculoskeletal and skin disorders and diseases. Basic investigations involve immunology; purine metabolism; skeletal muscle structure, function, metabolism and physiology; the structure, function, production, biochemistry and physiology of collagen, elastin, and other proteins of connective tissue; metabolic and hormonal changes in bone; prevention and treatment strategies for osteoporosis and related bone diseases, structural and biochemical changes in osteoarthritic cartilage and cartilage repair; novel imaging modalities for bone, cartilage, and connective tissues; new treatments for fractures and other musculoskeletal tissues including tissue engineering and gene therapy; orthopaedic implant science (materials, design, wear, osteointegration); bioimaging of musculoskeletal tissues; computer-assisted orthopaedic surgery and other computer-assisted musculoskeletal bioimaging and treatment interventions; the biomechanics of normal, arthritic and prosthetic joints; the structure, function, barrier properties, metabolism, and physiology of the skin. Exercise research related to musculoskeletal function, including the development of tools or behavior modification programs to enhance exercise in normal individuals or those with chronic diseases, and related behavioral and prevention research.

For additional information about areas of interest to the NIAMS, please visit our home page at http://www.niams.nih.gov.

Arthritis and Musculoskeletal and Skin Diseases

A. ***Rheumatic Diseases Branch.*** Supports basic and clinical research in the normal function and components of connective tissue and the immune system and their dysregulation in rheumatic, genetic, and inherited diseases of connective tissue. The goals are increased understanding of the etiology and pathogenetic mechanisms involved in rheumatic and degenerative disease of the joints and in the translation of these basic research findings to prevention, diagnosis, and treatment of disease. The research supported by the Program utilizes approaches emanating from relevant areas of genetics, biochemistry, cellular and molecular biology, biophysics, enzymology, immunology, pathology, physiology, behavioral medicine, and epidemiology.

   A description of other areas of research under investigation may be found at http://www.niams.nih.gov/rtac/funding/grants/ep3.htm.

B. ***Musculoskeletal Diseases Branch.*** Supports studies of the skeleton and associated connective tissues. Research areas supported through the Musculoskeletal Diseases Branch include bone diseases, bone biology, and orthopaedic research. Broad areas of interest include skeletal development, metabolism, mechanical properties, and responses to injury. Osteoporosis, a disease afflicting many of the Nation's growing population of older people, is particularly emphasized for investigation under this program. Among other diseases and skeletal disorders under investigation are osteogenesis imperfecta, a genetic disorder that leads to fragile, easily fractured bones; Paget's disease of bone, which results in irregular bone formation and subsequent deformity; genetic disorders of bone growth and development, such as osteopetrosis and the osteochondrodysplasias; vitamin D refractory

diseases; and rickets and osteomalacia. Other studies focus on the causes and treatment of acute and chronic injuries, including carpal tunnel syndrome, repetitive stress injury, low back pain and clinical and epidemiological studies of osteoarthritis. The Program supports development of new technologies with the potential to improve treatment of skeletal disorders and facilitate the repair of trauma in the normal skeleton. These include drugs and nutritional interventions, joint replacement, bone and cartilage transplantation, and gene therapy. In addition, bioengineering, sports medicine and musculoskeletal fitness are areas of special research emphasis.

A description of other areas of research under investigation may be found at http://www.niams.nih.gov/rtac/funding/grants/ep5.htm.

C. ***Skin Diseases Branch.*** Supports basic and clinical studies of the skin in normal and disease states. The wide range of skin diseases under study with NIAMS support includes keratinizing disorders such as psoriasis and ichthyosis, atopic dermatitis and other chronic inflammatory skin disorders, the vesiculobullous diseases such as epidermolysis bullosa and pemphigus, acne, and vitiligo.

A description of other areas of research under investigation may be found at: http://www.niams.nih.gov/rtac/funding/grants/ep6.htm.

1. Determinations of drug effects.
2. Determinations of effects of other therapies, including occupational and physical therapy modalities, spinal manipulation, bracing, transcutaneous nerve stimulation, acupuncture, and topical agents (e.g., capasicin).
3. Preventive strategies.
4. Development and validation of animal models for rheumatic, musculoskeletal (especially for herniated intervertebral disc and spinal stenosis), muscle and skin diseases.
5. Improvement and refinement of immunogenetic determinants of rheumatic diseases.
6. Development of novel and improved diagnostic methods and treatments for muscle, tendon, ligament, bone, and joint injuries, including overuse and repetitive motion disorders.
7. Devices and activities designed to prevent muscle, tendon, ligament, and joint injuries, including overuse and repetitive motion disorders.
8. Assessment techniques for musculoskeletal and skin diseases.
9. Functional and metabolic measures of the musculoskeletal system in normal, diseased and active states.
10. Development of novel implant designs, materials and surface coatings for musculoskeletal implants. Development of assessment strategies to detect implant failure, loosening, and osteolysis, and the development of novel technologies to prevent them.
11. Computer modeling, relevance to the musculoskeletal system.
12. Improved topical treatments of skin diseases and disorders.
13. Devices and computer programs for diagnosis or assessment of skin diseases.
14. Tissue culture models for skin diseases.
15. Artificial skin.
16. Photoprotective agents.
17. Improved treatment for bone diseases.
18. Measurement techniques for bone diseases.
19. Preventive measures for fractures.
20. Delivery systems for dietary supplements.
21. Novel delivery systems for therapeutic agents.
22. Development of novel or improved technologies for bone healing and repair. This includes, but is not limited to, the development of osteoinductive, osteoconductive, or a combination, technologies to facilitate bone healing/repair, and the development of improved or novel approaches to the use of autogenous, allograft, and bone graft substitutes.
23. Development of novel or improved technologies to facilitate the repair of articular cartilage, including, but not limited

to cartilage cell transplantation, use of stem cells, biodegradable scaffolds, growth factors, and refinements of currently existing technologies.

24. Development of novel technologies to improve the diagnosis, prevention, and treatment of acute and chronic low back pain.
25. Development of novel assessment technologies for identifying biomechanical inputs on bone and cartilage tissue at the cellular level, and identification of the corresponding physiological response.
26. Development of novel technologies leading to the use of gene therapy for selected musculoskeletal diseases and injuries.
27. Development of novel, non-invasive technologies to assess joint tissues, including articular cartilage and subchondral bone.

Markers of Osteoarthritis

The NIAMS seeks applications for the development and validation of standardized, sensitive assays for osteoarthritis markers in body fluids or tissue specimens. Osteoarthritis is the most prevalent musculoskeletal disorder, characterized by joint pain, tenderness, and functional disability. The percentage of Americans over 65 years of age is the fastest growing segment of the population, which is expected to reach 68 million people by the year 2010. A biochemical test for osteoarthritis would be particularly useful for early detection, assessment of disease severity and progression, and to monitor the effects of therapies.

Advances in the molecular biology, biochemistry, and metabolism of cartilage have stimulated the quest for appropriate markers of degradative and regenerative processes in osteoarthritis. Important new studies indicate that molecular fragments of cartilage-derived matrix molecules are present in the blood and joint fluid in osteoarthritis that have the potential to represent disease-specific markers. The increased rates of cartilage degeneration increase the concentration of matrix components in tissue and body fluids, thus reflecting changes in the rates of cartilage catabolism. Further, cartilage degeneration in osteoarthritis changes the type or structure of the molecules being synthesized by the chondrocytes. Thus, the presence of these neo-epitopes may be a marker of degenerative events within the tissue. Markers of metabolic changes in subchondral bone or other joint tissues in osteoarthritis are also be of potential interest.

The NIAMS is soliciting applications to test the potential application of a marker for osteoarthritis diagnosis, prognosis or severity and the standardization of a clinically relevant test. Successful applicants will provide a rational approach for the development of a practical and reliable assay for osteoarthritis disease marker(s) and determination of the sensitivity and specificity of the marker(s) in patient populations. The applications must include the rationale for the selection of the marker to be employed in the study. If a battery of markers will be utilized the basis of this approach must be clear and well justified. The assay systems as well as the methods of sample collection, storage, and handling must be clearly delineated. Marker levels must be validated against other methods of monitoring osteoarthritis, such as imaging techniques. The expected outcome of these studies is an osteoarthritis test that can be used in larger scale human trials.

Muscle Biology, Exercise Physiology and Sports Medicine

A. ***Muscle Biology Branch.*** Supports research on skeletal muscle, its diseases and disorders, and its central role in human physiology and exercise. Topics include the molecular structure of muscle and the molecular mechanisms that produce force and motion. An aim is understanding the alterations in muscle resulting from increased exercise regimens and, conversely, the atrophy that follows immobilization during injury or illness. Some of the specific areas of research covered by the Muscle Biology Branch include Muscle Physiology, Molecular Architecture, Muscle Membranes, Muscle Development and Specialization, Musculoskeletal Fitness and Adaptive Biology, Muscle Diseases, and Sports Medicine, Muscle Injury and Muscle Repair. Areas that may be of interest to small businesses include but are not limited to:

1. Muscle Structure and Function.

   Research on the application of biochemistry, molecular, and cell biology to muscle biology, including studies of membrane structure, function, and biosynthesis, lipid metabolism, membrane models, membrane transport, sub-cellular organization, organelles, cytoskeletal components, and cell division.

Development of new instruments and methods to facilitate studies on muscle function and physiology. Specific examples might include, but are not limited to, the following:

a. Development of methods and materials directed toward the solution of muscle cytoskeletal and membrane protein structures by x-ray diffraction, electron diffraction, and NMR spectroscopy.

b. New methods for the purification and reconstitution of muscle membrane proteins.

c. Development of monoclonal and/or recombinant antibodies to cytoskeletal and membrane proteins exhibiting high specificity and affinity and broad cross-species reactivity.

2. Muscle Fitness and Sports Medicine.

a. Improve measurement of muscle strength and balance, including refined instrumentation for biomechanical assessment of normal movement and posture.

b. Develop quantitative methods of assessing postural perturbations and forces relevant to activities of daily living.

c. Improve imaging and analytical techniques to measure skeletal muscle properties, (e.g., through MRI Imaging and Spectroscopy).

d. Imaging techniques which allow simultaneous imaging of muscle morphology and metabolism and blood flow.

e. Development of novel assays or modifications of currently existing assay of muscle metabolism for use with human biopsy samples.

f. Develop biosensors to detect changes in pressure, temperature, or physiological parameters associated with muscular activity.

g. Development of treatments for wound healing and improve general understanding of the natural healing process for muscle.

h. Develop antioxidant interventions to prevent oxidative damage during muscle use and overuse.

i. Develop cell culture models for rapid testing of treatments for muscle injury and wasting.

3. Development and Genetic Diseases.

a. Develop animal models that mimic the pathophysiology of the genetic human muscle diseases.

b. Develop gene vectors (viral and non - viral), promoter and enhancer elements and related methodologies that could be used for in vivo and ex vivo gene therapy for muscular diseases.

c. Develop cell lines and tissue cultures for replacement of muscle that has been damaged or destroyed.

d. Develop markers for muscle satellite cells and use them to characterize availability for muscle repair.

e. Develop techniques, equipment, and software to enable improved imaging of muscle development and specialization.

A description of other areas of research under investigation may be found at: http://www.niams.nih.gov/rtac/funding/grants/ep4.htm.

Other Research Topic(s) Within the Mission of the Institute

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NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)

The NIBIB supports hypothesis-, design-, technology- or problem-driven research relating to the discovery, design, development, translation and assessment of new knowledge in biomedical imaging and bioengineering. This research may utilize, for example, an organ or disease as a model system for development purposes. Also, several Institutes or Centers may collaborate on research of mutual interest.

For additional information about areas of interest to the NIBIB, please visit our home page at (http://www.nibib.nih.gov/). This site includes staff contact information by program area (http://www.nibib.nih.gov/about/directory/program_staff_areas.html). It also includes links to program announcements and requests for applications that highlight NIBIB areas of special emphasis (http://www.nibib.nih.gov/research/investigators.htm). In some cases, these announcements specifically mention the SBIR and STTR grant mechanisms, in other cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in many of these announcements.

NIBIB Extramural Science Programs support research and training in various areas of biomedical imaging and bioengineering.

Biomedical Imaging research supported by the NIBIB includes imaging device development, biomedical imaging technology development, image processing, imaging agent and molecular probe development, informatics and computer sciences related to imaging, molecular and cellular imaging, bioelectrics/biomagnetics, organ and whole body imaging, screening for diseases and disorders, and imaging technology assessment. Areas that may be

of interest to small businesses include, but are not limited to:

A. Development of imaging devices for evaluation of all levels of biological material from single-copy (oligonucleotides or proteins) to whole body, particularly development of small animal imaging models.

B. Development of improved imaging techniques in the areas of spatial and temporal resolution, speed of information acquisition, detectors, and contrast resolution.

   1. Development of new methods for obtaining accurate, 3-dimensional depth dose information for radiography.

   2. Development of new display technologies for digital imaging systems and methods for their characterization/assessment.

C. Development of methods that increase the information obtained from images.

   1. Development of image reconstruction algorithms and image pre-processing methods.

   2. Development of new techniques or application of existing techniques (e.g., image segmentation, registration, or filtering) to gain additional data from images.

D. Application of informatics and computer sciences to imaging.

   1. Development of new and effective strategies for classification and estimation, using synthesis and integration of multimodal imaging and modeling approaches with a priori information.

   2. Integration of information content from diverse imaging methods and databases for diagnostic application.

E. Development of improved organ and whole body image resolution and data display while maintaining or improving minimization of invasiveness, imaging and processing time, costs, and patient discomfort.

F. Establishment of novel imaging techniques to pinpoint signifying events that mark disease onset and define its biologic characteristics.

Bioengineering research supported by the NIBIB includes biomaterials, biomechanics and rehabilitation engineering, tissue engineering, medical devices and implant science, therapeutic agent delivery systems, biosensors, platform technologies, nanotechnology, mathematical models and computation algorithms, bioinformatics and medical informatics, remote diagnosis and therapy, image-guided interventions, and surgical tools and techniques.

Although not exhaustive, topics of interest for SBIR and STTR applications may include the following:

A. Development of biomaterials. Development of novel materials to mimic structural features of biological systems by incorporation of an understanding of natural systems. Development of biomaterials that incorporate biomechanical design features.

B. Application of biomechanics for the continued improvement in the design and development of implants, prostheses, and artificial organs.

C. Development of fabrication techniques including synthesis or milling techniques, controlled and designed crystallization methods, large-scale methods suitable for manufacturing purposes, controlled particle aggregation, and nanoparticle coating techniques.

D. Development of functional tissue or organ substitutes in vitro for implantation in vivo, or to remodel and regenerate tissue in vivo for the purpose of repairing, replacing, maintaining, or enhancing organ function.

E. Development of substrates or scaffolds for tissue growth and differentiation.

F. Development of material science methods for combinatorial chemistry.

   1. Development of paradigms and techniques based on combinatorial approaches for the design, synthesis, characterization, assay, and end-use evaluation of complex, novel molecular entities and interactions.

   2. Develop of analysis tools that complement combinatorial approaches, including high throughput screening, chemical analysis, and biological assay.

   3. Development of tools for information management and dissemination to cope with the large amount of data generated by combinatorial approaches.

G. Development of improved implant surfaces and interface processes. Development of

techniques that can follow depositions on biomaterial surfaces in vitro and in real time.

H. Development of improved biosensor technology including the design, fabrication, and characterization of non-fouling sensors to be used in biomedical research and medicine. Development of algorithms or equations that relate the biosensor transducer measurement to biologically or medically relevant information.

I. Application of nanoscience derived principles toward the development of nanoscale components or biomolecular processes in diagnostic and therapeutic devices.

J. Design and construction of engineered nanosystems that may utilize biological or biologically inspired elements. Implementation and delivery of nanoscale tools for the diagnosis and treatment of disease or to interface with specific tissues to improve function.

K. Development of new targeted and systemic drug and gene delivery systems to enhance the delivery, selectivity, and therapeutic effects of agents.

L. Development of algorithms, mathematical models, simulations and analysis of complex biological, physiological, and biomechanical systems.

M. Development of new techniques to collect and store quantitative data ranging from the genome to the organism and to elucidate functional dynamics in living cells and tissues with sensitivity down to the level of single molecules.

N. Development of methods to support the transfer and application of population-based health information in clinical settings.

O. Development of methods for structuring, managing, and analyzing large, distributed, networked, adaptive databases.

P. Development of visualization standards for 3-D image acquisition, for visualization parameters to categorize various tissues in 3-D models and for interpreting 3-D images.

Q. Development of new minimally invasive surgical tools and techniques, as well as techniques for tracking and placement of surgical tools in a stereotactic space.

R. Development of new medical technologies, including image-guided therapies, computer-assisted surgeries, and large-scale simulation modeling to improve surgical outcome.

S. Development of novel telehealth instrumentation or technologies that provide and support health care at a distance and can be applied to a broad spectrum of disorders and diseases.

Other Research Topic(s) Within the Mission of the Institute

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NATIONAL CANCER INSTITUTE (NCI)

In its attempt to eliminate suffering and death due to cancer by 2015, the National Cancer Institute promotes research that crosses the discovery, development, and delivery continuum and that addresses barriers to progress, forging partnerships, opening access to datasets and tissue resources, and more fully utilizing emerging technologies in genomics, proteomics, communications, and delivery of clinical and public health interventions. To achieve these goals, NCI seizes extraordinary scientific opportunities and creates and sustains funding mechanisms that support translational research.

NCI's SBIR and STTR programs focus on research, development and delivery and are critical to achieving the institute's goals. Research opportunities cited below are not all inclusive; those listed are "open-ended" to encourage submission of innovative projects that fit NCI's mission. For additional information, access the NCI homepage: http://www.cancer.gov/ and http://otir.nci.nih.gov/smallbusiness/small_sbir.html .

Center to Reduce Cancer Health Disparities

Established in March 2001, CRCHD is the cornerstone of the Institute's efforts to reduce the unequal burden of cancer in our society. A central goal of the Center is to translate research discoveries into policies and/or services aimed at reducing cancer-related health disparities in racial, ethnic, elderly and medically underserved communities. To learn more about the Center, please visit our website: http://crchd.nci.nih.gov.

The Center is interested in the following SBIR/STTR applications:

A. ***Communication.*** Training tools to help health professionals deal with issues concerning health literacy and cultural competency.

B. ***Health Care and Epidemiology.*** Computer software and hardware for hand-held data input and analysis devices; databases and other tools to study patterns of cancer care in underserved communities.

C. ***New Technology.*** Instrumentation to facilitate early detection and screening, including telemedicine and remote medical imaging, and bioengineering technology (including nanotechnology) applied to cancer detection and diagnosis in underserved communities.

D. ***Geographic Information Systems.*** Simple, low-cost mapping software to overlay cancer patterns with socioeconomic data, health system infrastructure, healthcare, personal behaviors, ethnicity, risk factors, and consumer profiling among underserved communities.

E. ***Human Genomics.*** Tools and technology for health care providers using cancer research developments from genomics, pharmaco-genetics and proteonomics for underserved populations.

For additional information, please email our SBIR/STTR Program Director at Taylorem@mail.nih.gov.

Division of Cancer Biology

The Division of Cancer Biology (DCB) plans and directs, coordinates, and evaluates a grant- and contract-supported program of extramural basic and applied research on cancer cell biology and cancer immunology, and cancer etiology, including the effects of biological, chemical and physical agents, in the promotion of cancer; maintains surveillance over developments in its program and assesses the national need for research in cancer biology, immunology and etiology; evaluates mechanisms of biological, chemical and physical carcinogenesis and subsequent tumor growth and progression to metastasis; tests for carcinogenic potential of environmental agents; serves as the focal point for the Federal Government on the synthesis of clinical, epidemiological and experimental data concerning biological agents relating to cancer; and maintains the necessary scientific management capability to foster and guide an effective research program. For additional information, please visit our home page at http://www.nci.nih.gov/dcb/dcbhom.htm.

A. ***Cancer Cell Biology.*** The Cancer Cell Biology Branch (CCBB) seeks to understand the biological basis of cancer at the cellular and molecular level. This research utilizes lower eukaryote and animal models, and animal and human tumor cells and tissues to analyze the mechanisms responsible for the growth and progression of cancer. Specific research and technologies supported by CCBB in this solicitation include but are not limited to the following:

1. Development of novel methods and tools to study key aspects of programmed cell death including its regulation and modulation.
2. Development of methods to identify and isolate tissue-specific stem cells.
3. Development of markers associated with specific cellular processes or differentiation.
4. Development of novel techniques, tools, and vectors to transfer functional genes, proteins, antibodies, etc. into intact cells or organisms.
5. New or improved technologies for the efficient microdissection of tumor tissue sections to isolate and preserve human cancer cells appropriate for research.
6. Development of human tumor cDNA library banks to study gene expression in cancer.
7. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
8. Generation of new or improved animal models or non-mammalian models (e.g. flies, worms) as research tools to study human cancers.

9. Generation of new inbred genetic animal models that transmit defective or altered cancer-related genes.
10. Development of novel technologies, methodologies, tools, or basic instrumentation to facilitate basic cancer research (research tools).
11. Development of methods and tools to study processes of protein trafficking, post-translational modification, and degradation.
12. Development of novel methods and tools for the analysis of intracellular organelles.
13. Development of novel methods and tools to determine intracellular gradient status.
14. Improved extraction methodologies and tools for tumor specimens for the subsequent analysis of DNA, RNA, and proteins.
15. Development of new or improved methods to isolate intact cellular regulatory complexes.
16. Development of novel methods and tools to examine key cellular communication pathways.

B. ***Cancer Etiology.*** The Cancer Etiology Branch (CEB) supports research that seeks to determine the role of chemical, physical and biological agents as factors or cofactors in the etiology of human and animal cancer. The biological agents of primary interest are DNA viruses, RNA viruses, AIDS and AIDS-associated viruses, although the research may encompass all forms of life including bacteria and other microbial agents associated with cancer and use animal models of cancer and cancer vaccines. Chemical Carcinogenesis studies are concerned with cancers initiated or promoted by chemical or physical agents. A wide range of approaches are supported, including studies of the genetics of cell transformatioin, mutagenesis, tumor promotion and DNA damage, as well as studies of basic biochemistry and molecular biology of oncogenic and suspected oncogenic agents, viral oncogenes and associated tumor suppressor genes, pathogenesis and natural history studies, animal models, and preventive vaccine research. Mechanistic studies are encouraged in areas such as metabolism, toxicity and physiological distribution of carcinogens, genetics and regulation of enzymes, biochemical and molecular markers, and organ and cell culture systems and animal models. Also of interest are studies on cancer etiology by environmental chemicals, tobacco consumption and exposure, nutritional hazards, alcohol, asbestos, silica, and man-made fibers. CEB supports studies on endogenous exposure to steroid hormones and the generation of oxygen radicals during normal metabolism, studies on phytoestrogens and xenoestrogens and their impact on the metabolism of endogenous estrogens. In addition, CEB supports the development of analytical technologies to facilitate studies relating to carcinogenesis and mutagenesis. Specific research and technologies supported by CEB in this solicitation include but are not limited to the following:

1. Development of reagents, probes, and methodologies to evaluate the etiologic role of oncogenic viruses and other microbial agents (such as bacteria) in human cancer.
2. Development of novel in vitro culture techniques for oncogenic viruses or other microbial agents associated with or suspected of causing human cancer.
3. Development of sensitive, simplified diagnostic kits or reagents for the detection of oncogenic viruses or other microbial agents.
4. Development and characterization of animal models for studies of the mechanism of cancer induction by viruses or other microbial agents. The animals should faithfully mimic the human diseases associated with the virus or other microbial agent.
5. Development of methods (e.g., new-anti-microbial compounds, new vaccine approaches) to avert the induction of neoplasia in humans and animals by oncogenic viruses or bacteria.
6. Development of other novel technologies, methodologies or instrumentation to determine the role of biological agents, especially viruses, in the etiology of cancer.
7. Development and validation of methods for food treatment, preparation, or processing that will reduce or eliminate carcinogen/mutagen content.

8. Development of rapid analytical techniques for the qualitative and quantitative detection and screening of xenobiotics, chemical contaminants, and carcinogens/mutagens in human foods and biological and physiological specimens.
9. Development of in vitro and in vivo models for basic studies of carcinogenesis in specific organ systems, such as the pancreas, prostate, ovary, central nervous system, kidney, endometrium, stomach, and upper aerodigestive tract.
10. Development of methods for the production of carcinogens, anticarcinogens, metabolites, biomarkers of exposure, oxidative damage markers, and DNA adducts, both labeled and unlabeled, which are neither currently available commercially nor offered in the NCI Chemical Carcinogen Reference Standard Repository. The production of these compounds, in gram quantities, is desired for sale/distribution to the research community.
11. Development of methods for detection, separation, and quantitation of enantiomeric carcinogens, metabolites, adducts, and biomarkers of carcinogen exposure.
12. Development of monoclonal antibodies that are specific for different carcinogen-nucleoside adducts and demonstration of their usefulness in immunoassays. Of particular interest are antibodies to alpha-beta unsaturated carbonyl compounds (such as acrolein and crotonaldehyde) which can form exocyclic nucleoside adducts with DNA, and immunoassays for carcinogen/protein adducts as potential biomarkers of exposure.
13. Development of immunoassays using monoclonal antibodies that are specific for different polymorphs of Phase I and II carcinogen-metabolizing enzymes and repair enzymes. Included, but not limited to, are antibodies to the cytochrome P450 isozymes, glutathione S-transferases, and N-acetyl transferases.
14. Development of rapid, sensitive, and quantitative assays for the identification and measurement of androgens, estrogens, phytoestrogens, and xenoestrogens in complex biological matrices.
15. Development of rapid analytical techniques for the direct measurement of ligand-protein receptor interactions and determination of binding coefficients.
16. Development of analytical instrumentation for the detection and quantitation of extremely low levels of Tritium (3H) or 3H and Carbon-14 (14C) from biological samples. Of particular interest is the development of small-sized, accelerator-based mass spectrometry equipment capable of measuring down to, or below, contemporary background levels of 3H and 14C that would make this sensitive technique more widely available to research groups. The design and development of technologically improved and miniaturized individual components, including ion source, sample preparation (autosampling apparatus), accelerator, and mass spectrometric detectors, are also solicited.
17. Synthesis of selective suicide inhibitors of cytochrome P450 isoforms and selective arachidonic acid pathway inhibitors/ enhancers for basic biochemical studies and anticarcinogenic potential.
18. Development of invertebrate animal models (such as Drosophila, C. elegans, clam, and sea urchin) for the study of environmental chemicals and/or hormonal carcinogenesis.
19. Development of more efficient and reliable methods of preserving valuable animal model gene stocks by innovative in vitro techniques.
20. Development of a defined diet for support and maintenance of aquatic and marine fish models of cancer including but not limited to swordtail, zebrafish, medaka, mummichog, guppy, Fugu, and Damselfish.
21. Development of serum free tissue culture media for aquatic and marine fish models of cancer.

C. ***Cancer Immunology and Hematology.*** The Cancer Immunology and Hematology Branch (CIHB) supports a broad spectrum of basic research focused on the earliest stages of hematopoiesis and tracing the molecular events that lead to the development of all the

functional elements of the immune system and, when errors occur, to the development of leukemias and lymphomas. Most research of interest falls into three major areas. The first is the immune response to tumors to include studies of all of the cells (T, B, NK, antigen-presenting, and other myeloid cells) and secreted molecules (antibodies and cytokines) of the immune system that can recognize and affect tumor growth. Emphasis is placed on the regulatory mechanisms responsible for the failure of immune response to eradicate most tumors under normal conditions, and the development of strategies to circumvent these mechanisms. A second major area of interest examines the biology of hematopoietic malignancies to describe the detailed reasons underlying cell's failure to respond to normal growth controls and to develop novel approaches to prevention or therapy. The third distinct area supported is the basic biology of bone-marrow transplantation, including studies of host cell engraftment, graft-versus-host disease, and the basis of the graft-versus-leukemia effect. Specific research and technologies supported by CIHB in this solicitation include but are not limited to the following:

1. Development of improved or novel monoclonal antibody technologies including improvements of methodologies for fusion, production of novel cells as fusion partners, selection and assay of antibody producing clones, and production of new and improved monoclonal antibodies.
2. Synthesis, structure and function of antibodies capable of reacting with tumor cells, agents that induce tumors, agents used in the treatment of tumors, and agents used in the treatment of tumors.
3. Development of in vivo animal models systems that can be used to study the immune response to tumors and the mechanisms of immunotherapy.
4. Synthesis, structure and function of soluble factors that participate in, activate and/or regulate hematopoietic cell growth and the immune response to tumors, including interferons, other lymphokines and cytokines (interleukins), hematopoietic growth factors, helper factors, suppressor factors and cytotoxic factors.
5. Application of biochemical, molecular biological and immunological techniques for identifying tumor antigens that are good targets for the development of vaccine-type strategies of cancer immunotherapy.
6. Development of techniques to enhance the immune response to tumors, including modification of tumor cells and/or antitumor lymphocytes to facilitate cancer vaccine strategies.
7. Development of improved methodology for manipulating bone marrow inoculum to decrease the incidence of graft-versus-host disease without increasing the risk of graft failure or leukemic relapse.
8. Development of improved methodology for increasing the number of peripheral blood stem cells available for harvest for use in transplantation, including improved methods of identifying and removing residual leukemic cells in the autologous transplant setting.
9. Development of methods to identify and define human minor histocompatability antigens.
10. Development of novel culture systems to improve the expansion of lymphocytes.
11. Development of the combination of cell culture and other research tools to better expand human hematopoietic stem cells.
12. Development of improved techniques for computational simulation/modeling of biological processes involved in immunologic defenses against tumor cells such as signal transduction, cell cycle progression, and intracellular translocation.
13. Development of other novel technologies, methodologies or instrumentation to facilitate basic research in either tumor immunology or cancer hematology.
14. Development of molecular, cellular or biochemical techniques to isolate and/or characterize tumor stem cells from hematologic malignancies.

D. ***DNA and Chromosome Aberrations.*** The DNA and Chromosome Aberrations Branch (DCAB) seeks to study the genome at the DNA and chromosome level, including discovery of genes at sites of chromosome breaks, deletions, and translocations; DNA repair;

structure and mechanisms of chromosome alterations; epigenetic changes; radiation- and chemical-induced changes in DNA replication and other alterations; and analytical technologies. Specific research and technologies supported by DCAB in this solicitation include but are not limited to the following:

1. Development of new, improved technologies for characterization of chromosomal aberrations in cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for chromosome aberrations in cancer.
3. New or improved technologies to increase accuracy of karyotypic analyses of tumor specimens.
4. New or improved methods to mutate or replace genes at specific sites in intact cells.
5. Development of new, sensitive methods to assess the methylation status of genes.
6. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
7. Technologies for assaying for mammalian genes relevant to repair of damage induced by exposure of mammalian cells to ionizing and non-ionizing radiations, with special emphasis on human cells.
8. Methods/approaches to study the repair of DNA lesions induced by exposure of mammalian cells to ionizing radiations (both high- and low-LET).
9. Development and characterization of human cell lines with specific DNA-repair deficiencies.
10. Development of genetic constructs that utilize radiation-responsive regulatory genes to control the expression of targeted structural genes in mammalian cells.
11. Development of new methods/technologies to assay transcription factor binding sites across whole genomes.
12. Use of RNAi and siRNA in the development of novel methods and tools for the study of gene expression, gene silencing, gene regulation, and genome-wide screening in cells and tissues.

E. ***Mouse Models of Human Cancers Consortium.*** The Mouse Models of Human Cancer Consortium is a program based in the Office of the Director, DCB. The Consortium has the important goal of providing mouse cancer model-related resources and infrastructure to the research community, in part through various outreach activities. The outreach requirement generates the need for innovative educational or informational materials that convey the content of Consortium meetings and symposia, or document hands-on workshops in which models or techniques that are pertinent to mouse modeling are demonstrated. The instructional materials may be CD-ROMs, videotapes, Web-based interactive programs, or other media.

F. ***Structural Biology and Molecular Applications.*** The Structural Biology and Molecular Applications Branch (SBMAB) focuses on structural and molecular studies to explore the processes of carcinogenesis and tumorigenesis. Areas of interest include structural biology, genomics, proteomics, molecular and cellular imaging, enzymology, bio-related and combinatorial chemistry, and bioinformatics, as they apply to cancer biology. Interests also include modeling and theoretical approaches to cellular and molecular dimensions of cancer biology. Specific research and technologies supported by SBMAB in this solicitation include but are not limited to:

1. Development of new technologies to facilitate the analysis and determination of the molecular structure of biomolecules associated with cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for gene identification.
3. Development of systems that will automate the technology of culturing or assaying single cells.
4. New or improved technologies for efficient microdissection of tumor tissue sections and the development of tissue arrays.
5. Improved extraction techniques for tumor specimens for subsequent DNA, RNA, and protein analyses.

6. Rapid methods to isolate intact complexes of regulatory proteins and to separate and identify the proteins.
7. New or improved technologies for the preservation of small amounts of DNA/RNA/protein samples
8. Development of new techniques and vectors for transfer of genes, proteins, and antisense molecules into cells.
9. Generation of software and computer models for the prediction of macromolecular structure and function.
10. Development of bioinformatic tools for the study of cancer biology including facilitating genome data, gene "mining," cluster analysis, and data base management.
11. Development of novel gene technology (e.g., microarray, differential display technology) for measurement of differential gene expression levels and functional genomics studies.
12. Development of novel proteomic tools for the analysis of protein expression in cancer biology.
13. Computer-based methodologies to assist in the understanding of signal transduction and cancer biology.
14. Methodologies and techniques for the imaging of macromolecules in vitro and in vivo.
15. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer biology.
16. Develop new approaches and technologies for the structural determination of large biomolecular complexes.
17. Development and integration of nanotechnology approaches and tools in basic cancer biology research.
18. Application and development of novel approaches for in vivo and in vitro modifications of protein expression in cells and tissues, e.g. RNAi.
19. Mathematical and theoretical models for the understanding of cancer biology.
20. Development of new software and lab analysis tools that will improve the recording and collection of data and experimental protocols in order to facilitate cancer biology research.

G. ***Tumor Biology and Metastasis.*** This branch supports research that seeks to understand the interactions of cancer cells with the tumor and/or host microenvironment in order to delineate the molecular mechanisms and signaling pathways of tumor angiogenesis and lymphangiogenesis, cell migration and invasion, tumor progression, and metastasis. This includes examination of cell-cell and cell-matrix interactions, and the roles played by cell growth factors and cytokines, adhesion molecules, cytoskeleton and the nuclear matrix, and matrix-degrading enzymes, as well as studies on the pathology and biology of solid tumors and tumor bearing animals, and the development of technology to facilitate these studies. Emerging areas of emphasis are the microenvironment created by inflammation and the inflammatory signaling molecules in tumor initiation and progression and the role of somatic stem cells in determining tumor progression and metastatic behavior. Stem cell motility, positional information cues from surrounding tissue and adhesion properties together with issues of epithelial-mesenchymal transitions related to cancer progression are supported. Emphasis is also placed on the role of the extracellular matrix and tissue microenvironment during development and tissue morphogenesis, and on the role of glycoproteins in tumor growth, invasion, and metastasis. The branch also focuses on the function of steroid hormones, their receptors and coregulators during tumor growth and progression. Models utilized in these studies may include animal models, tumor tissues/cells, their components, or their products. The development of organotypic models that closely mimic in vivo models is encouraged. Specific research and technologies supported by TBMB in this solicitation include but are not limited to:

1. New technical strategies to identify and assess the function of components of the extracellular matrix.
2. Development of new in vitro cancer models to study the pathology and biology of solid tumors and tumor bearing animals.
3. New in vivo models of angiogenesis, lymphangiogenesis, cancer progression and metastasis.

4. Development of technologies to identify novel factors that modulate angiogenesis and lymphangiogenesis.
5. Identification of genes and/or enzymes associated with glycosylation in tumor cells.
6. Identification of novel coregulators of nuclear steroid receptor superfamily.
7. Development of improved techniques for computational simulation/modeling of biological processes involved in malignant transformation, persistence, or invasion, such as signal transduction, cell cycle progression, and intracellular translocation.
8. Development of new assays or methods to evaluate tumor cell invasiveness.
9. Development of new assays or methods to study molecules and pathways involved in cell-to-cell signaling or communication.
10. Development of appropriate new animal, cellular or organotypic models to study tumor stroma interactions, 3-D models that closely mimic *in-vivo* conditions.
11. Study roles of cytokines/growth factors released by host cells during inflammation, invasion, tumor progression and metastasis.

Division of Cancer Control and Population Sciences

The Division of Cancer Control and Population Sciences conducts basic and applied research in the behavioral, social, and population sciences, including epidemiology, biostatistics, and genetics that, independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality. Laboratory, clinical and population-based research, and health care are translated into cancer prevention, detection, treatment, and rehabilitation activities that cross the life span and the entire process of carcinogenesis, from primary behavioral prevention in youth, to screening, treatment, and survivorship. For additional information, please visit our home page at http://dccps.nci.nih.gov.

A. ***Epidemiology and Genetics.*** The Epidemiology and Genetics Research Program supports research in epidemiology, biometry, genetic epidemiology, molecular epidemiology, nutritional epidemiology, infectious epidemiology, environmental epidemiology, computing methodology, and multidisciplinary activities related to human cancers.

The updated topics of interest to the Epidemiology and Genetics Research Program (EGRP) are:

- **Tools for assessment of exposures and biomarkers:**
  - Development of methods for measuring biomarkers of human exposure or susceptibility, and of nutritional status, and methods for monitoring changes in biomarkers for use in cancer epidemiologic studies.
  - Development of new or improved devices for quantitative measurement of human exposure to environmental carcinogens for epidemiologic studies.
  - Development of methods to evaluate potential cancer clusters for epidemiologic studies.
- **Tools for cancer epidemiology studies:**
  - Development of tools to model cancer risks from environmental and occupational agents.
  - Development of software for electronic capture of risk factor data for cancer epidemiologic studies.
  - Build consumer-friendly risk prediction models from epidemiologic data.
  - Development of software for tracking biological specimens for cancer epidemiologic studies.
  - Development of software for electronic identification, screening, and recruitment of participants, especially minorities, into epidemiologic studies.
  - Development of Web-based data collection or applicable bioinformatics tools for cancer epidemiology.
  - Development of software or methods for rapid case ascertainment of cancers.
  - Development of geographic information systems with special visualization techniques for the simultaneous

assessment of environmental exposures and health outcomes.

- Development of tools using publicly available data to identify population-based controls for epidemiologic studies.
- Development of software for analysis of DNA methylation biomarkers for early detection of prostate or breast cancers with use of specimens from biorepositories.

For more information on this program please go to http://epi.grants.cancer.gov.

B. ***Multimedia Technology and Health Communication in Cancer Control.*** The NCI promotes communication about and dissemination of information about cancer. Toward these efforts, the Behavioral Research Program (BRP) uses its SBIR/STTR Multimedia Technology Health Communication Program to fund translational research using a variety of multimedia.

The objectives of this program are to (1) *fund* science-based, theory-driven, user-centered grants and contracts to translate cancer research into programs, interventions, systems, networks, or products needed by professionals or the public to reduce cancer risk or improve the quality of life of cancer survivors; (2) *promote the use of* innovative media technology and/or communication approaches in cancer prevention and control applications used in medical and community settings; (3) *improve* communication behaviors of primary care professions, patients, and care-givers in cancer-related matters; (4) *promote* organizational infrastructures changes that promote the use of products developed in the program; (5) *promote* the development of system models; and (6) *expand* the methods for evaluating ehealth research and developed products.

Investigators interested in applying for grants in this SBIR program should access: http://cancercontrol.cancer.gov/hcirb/sbir/ for a list of topics that address current gaps in ehealth research. This list replaces previously listed research categories. This site also provides important program requirements and SBIR information.

For questions, contact the Program Director at cd34b@nih.gov.

Division of Cancer Treatment and Diagnosis

The Division of Cancer Treatment and Diagnosis funds research into the development of tools, methodologies and therapeutic agents that will better diagnose, assess, cure and effectively treat cancer. We support a spectrum of research projects from preclinical exploratory research and development through clinical trials.

A. ***Cancer Diagnosis.*** The Cancer Diagnosis Program (CDP) supports the development of technologies, reagents, instrumentation, and methodologies to improve cancer diagnosis or prognosis or to predict or assess response to therapy. This does not include technologies for imaging of patients. CDP also supports the adaptation or improvement of basic research technologies for use as clinical tools. Technologies supported by CDP may be designed to work with tissues, blood, serum, urine, or other biological fluids. Technologies supported by CDP include but are not limited to the following:

1. Technologies for comprehensive and/or high throughput analysis of molecular alterations at the level of DNA, RNA, or protein. Includes for example, mutation detection systems, gene expression arrays, systems for monitoring epigenetic changes (alternative splicing or methylation), high throughput proteomics (including post-translational modification and protein-protein interactions and methods for protein quantitation).
2. Micro-electro mechanical systems (MEMs) and other nanotechnologies for the analysis of DNA, RNA, or protein (e.g., micro-capillary systems, lab on a chip applications, micro-separation technologies).
3. Mass spectrometry for the analysis of nucleic acids or proteins.
4. Discovery and development of new or improved diagnostic markers or probes targeting changes in DNA, RNA, or proteins, including the generation of molecular diversity libraries by phage display and other combinatorial techniques, and affinity-based screening methods.

5. cDNA library technologies, including improved methods for generating high quality cDNA clones and libraries and methods for generating high quality cDNA from tissues (including archived specimens).
6. Resources for clinical research.
   a. Instruments, technologies or reagents for improved collection, preparation, and storage of human tissue specimens and biological fluids.
   b. Improved methods for isolation and storage of DNA, RNA, or proteins.
   c. Tissue and reagent standards: development of standard reagents such as representational DNA, RNA, and proteins and standard tissue preparations to improve the quality of or facilitate the validation of clinical laboratory assays.
   d. Methodologies for directed micro-sampling of human tissue specimens, including for example, new or improved methodologies for tissue microarrays.
7. Tissue preservation: fixatives and embedding materials or stabilizers that preserves tissue integrity and cellular architecture and simultaneously allows molecular analysis of DNA, RNA, or proteins.
8. Bioinformatics.
   a. Methods for acquisition and analysis of data associated with molecular profiling and other comprehensive molecular analysis technologies, including for example, analysis of microarray images and data as well as methods to combine, store and analyze molecular data produced by different techniques (e.g., combined analysis of proteomics and gene expression data).
   b. Methods for collecting, categorizing or analyzing large data sets containing pathology data or histological images and associated clinical or experimental data, including for example, tumor marker measurements, tissue microarray data, and other relevant biological information.
   c. Software/algorithms to interpret and analyze clinical and pathology data including methods that relate data from clinical databases to external data sources. Includes for example, neural networks, artificial intelligence, data-mining, data-trend analysis, patient record encryption protocols, and automatic diagnostic coding using standard nomeclatures.
   d. Informatics tools to support tissue procurement and tissue banking activities.
9. Statistical methods and packages designed for data analysis including correlation of clinical and experimental data.
10. Automated Cytology.
    a. High resolution image analysis for use with specimens (e.g., blood, tissues, cells) and tissue microarrays.
    b. Instrumentation including microscopy and flow cytometry.
    c. CGH, FISH, immunohistochemical staining and other hybridization assays using probes with fluorescent or other novel tags.
    d. Methods for single cell isolation and sorting.
    e. Methods for single cell classification and analysis.
11. Instrumentation for the detection and diagnosis of tumors, including endoscopy and magnetic resonance spectroscopy (MRS).
12. Immunoassays using monoclonal, polyclonal, or modified antibodies. Affinity-based binding assays using libraries of aptamers including chemical ligands, small peptides or modified antibodies.

For additional information about areas of interest to the CDP Technology Development Branch, visit our home page at: http://cancerdiagnosis.nci.nih.gov.

B. ***Biochemistry and Pharmacology.*** Preclinical and Exploratory Investigational New Drug (IND) studies designed to improve cancer treatment. General areas of interest: Discovery of new drugs or drug combinations and treatment strategies, selective targeting, development of clinically relevant preclinical models,

pharmaceutical development, ADME (absorption, distribution, metabolism and excretion) studies and toxicologic evaluations, understanding mechanisms of drug actions (responses to therapies), and preventing and overcoming drug resistance. Areas of current emphasis: Molecular targeted approaches, including application of safety and efficacy biomarkers to the discovery and development of drugs; application of advanced technologies, such as nanotechnology and imaging technologies, to improved assays for quantitation of safety and efficacy biomarkers; approaches that reduce costs and increase speed of preclinical drug development; and approaches that will lead to "personalized medicine," including better predictions of drug response and adverse reactions, drug-drug interactions, and drug efficacy monitoring. For additional information, please visit our home page at http://dtp.nci.nih.gov and select "Grants/Contracts."

1. *Drug Discovery*.

   a. Design and synthesize novel compounds for evaluation as potential anticancer agents. Synthesize simpler analogs of complex antitumor structures that retain antitumor activity.

   b. Develop computer modeling and biophysical techniques such as x-ray crystallography and NMR spectroscopy.

   c. Design prodrugs of anticancer agents that are selectively activated in cancer cells.

   d. Discover new anticancer agents that exploit unique properties of tumors, that induce or modulate apoptosis, or that induce or modulate differentiation.

   e. Design and synthesize anticancer prodrugs, latent drugs, or modifiers of cancer drug metabolism or excretion.

   f. Develop ways to produce adequate quantities of promising natural products or natural product derivatives through total synthesis.

   g. Develop scale-up and manufacturing technology for the synthesis of materials with promising anticancer potential.

   h. Develop chemical libraries for anticancer drug screening programs. The generation of small molecular weight libraries (<700 MW, e.g., non-polymeric organic molecules, transition-state analogs, cyclic peptides, peptidomimetics) is encouraged.

   i. Develop and apply technologies in genetics, genomics, proteomics, glycomics, lipidomics, metabolomics, and systems biology to the discovery of potential drug targets associated with multiple pathways or networks. Design and optimize agents that block or activate targets that are likely to control, retard or kill cancer cells.

2. *Drug Evaluation*.

   a. Develop and evaluate anti-metastatic and/or anti-angiogenesis agents or strategies, including combination therapies, in appropriate model systems.

   b. Develop and evaluate anticancer gene therapy in appropriate model systems. The development of new gene delivery approaches is encouraged.

   c. Develop novel or improved in vitro and in vivo test systems. There is a special need for new types of in vivo tumor models, such as orthotopic tumor models, models using transgenic or gene knockout animals, and models to evaluate agents that induce differentiation or apoptosis.

   d. Develop strategies to detect, prevent, or overcome drug resistance.

   e. Develop novel treatment strategies such as extra corporeal treatment.

   f. Develop new assays based on molecular targets, especially those that may be amplified or altered in cancer cells. For example, develop assays for agents that interact with oncogenes, suppressor genes, signal transduction pathways, transcription factors, promoters. Assays based on molecular targets that can be adapted for high volume screening of chemical libraries are especially encouraged as well as in vivo models, which can be used for "proof of concept" (i.e., validating

selectivity of the agent for the target and confirming that modulation of the target results in antitumor activity).

g. Develop cost-effective and useful techniques to improve in vitro cell culture methodology, such as the development of automated systems, serum-free media, or carbon dioxide-free buffering systems to stabilize cell culture performance.

h. Identify and employ novel targets for antitumor drug discovery utilizing non-mammalian genetically defined organisms, such as fruit flies, worms, zebrafish and yeast.

i. Develop and apply technologies such as microarrays, proteomics or RNAi to improve the efficiency of drug discovery.

j. Develop cell lines that contain bioluminescent reporter genes, such as luciferase, that can be controlled by activating specific promoters.

3. *Pharmaceutical Development*.

a. Develop new methods to improve drug solubility for administration of promising antitumor compounds, such as water miscible nontoxic water solubility enhancing agents.

b. Develop bioavailable alternatives to the intravenous delivery of cytotoxic chemotherapy. For example, develop new excipients to enhance oral bioavailability of anticancer agents.

c. Develop biocompatible additives and excipients for highly concentrated proteins and peptide formulations to enhance bioavailability and stability suitable for subcutaneous delivery of agents.

d. Develop improved methods to reduce thrombophlebitis and other related side effects observed following intravenous injection of some anticancer drugs.

e. Develop new and innovative techniques for sterilization of parenteral dosage forms.

f. Develop in vitro and in vivo models to predict human oral bioavailability of anticancer drugs.

g. Develop practical delivery systems involving nanotechnology (dendrimers, nanoparticles, nanoshells, etc.) or other strategies to deliver anticancer drugs to specific target sites.

h. Develop new technology to manufacture liposomal and intravenous emulsions in an environmentally friendly manner and in accordance with OSHA standards.

i. Develop additives and/or processes to eliminate cold chain storage of biotherapeutic agents, especially vaccines.

4. *Toxicology and Pharmacology*.

a. Develop biochemical or molecular (genomic, proteomic, or metabolomic) response profiles of specific target organs (e.g., bone marrow, gastrointestinal tract, liver, kidney, heart, lung) to permit rapid identification of toxic effects resulting from anticancer drug administration.

b. Develop clinically relevant in vitro and/or in vivo tests for estimation and prediction of gastrointestinal toxicity, neurotoxicity (central and peripheral), cardiotoxicity, hepatotoxicity, nephrotoxicity and pulmonary toxicity.

c. Correlate in vivo and in vitro models for organ toxicity as described above in 4b. Validate for various anticancer drugs.

d. Develop drug metabolism (Phase I and Phase II) profiles for anticancer agents in human, mouse, rat and dog liver S-9, microsomes and slices.

e. Develop systems to identify toxic effects of drugs by characterizing reactions with biomolecules or receptors.

f. Develop in vitro tests to detect, qualify and quantify toxic effects of antineoplastic drugs. Develop techniques for determining individual variations in drug responses due to genetic polymorphisms or other factors.

g. Develop personal computer programs for pharmacokinetics models capable of predicting drug behavior in humans from preclinical pharmacokinetics data

in mice, rats, dogs, and non-human primates.

h. Investigate and develop techniques for relating specific enzyme activities (both catabolic and anabolic) to body sizes of different species.

i. Investigate techniques that would allow parameters, e.g., Km and Vmax for enzymes, to be scaled from preclinical to clinical models.

j. Develop analytical strategies applicable to the quantitation of potent anticancer drugs in biological fluids at the pg/ml level, e.g., Bryostatin.

k. Develop non-invasive techniques to determine drug distribution in various animal models.

l. Evaluate interspecies transporter distribution and its impact on pharmacokinetic parameters, e.g., the impact of pharmacogenetic variation in biodistribution.

m. Determine optimal pharmacokinetic sampling schedules for use in dose titration/pharmacodynamic assessment by integrating information such as pre-clinical pharmacokinetic data, physico-chemical drug properties and mechanism of action.

n. Develop an in vitro/in situ system for high throughput drug screens for oral bioavailability.

o. Develop and deliver organ specific chemo-protective agents.

p. Develop and evaluate rapid, cost-effective methods, including biochemical, functional multiplexed, imaging, nanotechnology-based, and microfluidics-based assays, to quantitate surrogate endpoints for determination of doses, dosing schedules, safety, and efficacy of drugs.

q. Identify and develop biomarkers to evaluate drug activities and toxicities.

r. Develop assays in support of Exploratory Investigational New Drug Studies using biomarkers or other appropriate endpoints.

s. Develop, standardize, and validate cost-effective tools for obtaining comprehensive ADME and toxicology profiles that may better predict the performance of drugs in humans.

t. Develop and analytically validate assays or tools for measuring safety, efficacy, and dosing biomarkers.

5. *Animal Production and Genetics*.

   a. Investigate alternatives to expensive barrier systems for exclusion of pathogens from rodent colonies, e.g., by use of micro-isolator cages, and evaluate their performance.

   b. Develop and evaluate specialized shipping containers for pathogen-free animals.

6. *Natural Product Discoveries*. Note that execution of projects in most of these topic areas will require collaboration and signed agreements with countries where the source organism was originally collected.

   a. Develop techniques for the study of non-culturable organisms in order to identify antitumor agents.

   b. Develop techniques for the genetic and biochemical characterization and the manipulation of biosynthetic pathways to create leads. Use combinatorial biosynthesis to generate libraries of un-natural natural products as drug leads.

   c. Use genetic techniques for the identification of microbial consortia, and for the identification and isolation of genes controlling the biosynthetic pathways producing potential antitumor agents.

   d. Express biosynthetic pathways from microbes or microbial consortia that are known to produce antitumor agents, but in organisms amenable to standard fermentation techniques.

   e. Investigate new biological methods, such as tissue culture, aquaculture, hydroponics, etc., for the production of natural products as potential anticancer agents.

   f. Develop new systems of large-scale production using biotransformation, tissue or cell culture, biotechnology,

modification of the chemical ecology of producing organisms, etc., in order to produce the large quantities of anticancer drugs needed for preclinical or clinical development.

g. Develop methods for the isolation, purification, identification, cultivation, and extraction of microorganisms from unusual marine or terrestrial habitats for antitumor screening. Examples are gliding bacteria, barophilic, endophytic, thermophilic, and tropical canopy organisms.

h. Investigate newer methods of isolation and purification, such as super-critical fluid extraction and chromatography, centrifugal countercurrent chromatography or affinity-based separations, in the isolation and purification of natural products with anticancer activity.

i. Develop simple immunoassays that can be used to monitor the levels of natural products of interest in simple extracts of the relevant raw material. These assays should be capable of being developed for use “in the field” and also in developing countries.

j. Develop analytical and biological methods for isolation, purification and validation of active constituents identified from alternative medicine and complementary studies; use of these purified constituents alone or in combination with conventional anticancer agents.

7. *Data Management Systems*.

a. Develop data support systems for chemical library programs.

b. Develop bioinformatics tools to accelerate the identification, functional understanding and validation of drug targets.

c. Develop bioinformatics tools to predict ADME and toxicology characteristics of drug candidates.

d. Develop “data mining” strategies such as neural networks.

e. Develop algorithms for determining optimal drug combinations and for prediction of optimal effectiveness of individual agents.

f. Develop bioinformatics tools to support a systems biology approach to drug discovery and development.

g. Develop bioinformatics tools to support genomic/proteomic and other "omics" profiling experiments in support of drug discovery and development.

C. ***Cancer and Nutrition.*** Research to improve the methodology of nutritional assessment in a cancer population. Innovative approaches to evaluate the contribution of nutritional status to response to cancer treatment.

1. Research to improve the methodology of nutritional assessment in a cancer population.

2. Develop means to evaluate the contribution of nutritional status to response to cancer treatment.

D. ***Clinical Treatment Research.*** Clinical research studies designed to improve cancer treatment. Emphasis is on clinical trials for the evaluation of new therapeutic agents, development of assay systems to measure patient response to chemotherapy, development of prognostic assays, and development of methods of analysis and management of clinical trials data. Studies designed to improve human subject protections for patient access to clinical cancer trials.

1. *Evaluation of New Cancer Therapies*.

a. Conduct clinical trials for the evaluation of new therapeutic agents or modalities of treatment employing drugs, biologics or surgery.

b. Clinical trials using “unconventional therapies,” including, but not limited to, behavioral and psychological approaches, dietary, herbal, pharmacologic and biologic treatments, and immuno-augmentative therapies.

c. Development and evaluation of new clinical approaches using gene transfer or gene therapy technologies.

d. Development and evaluation of new clinical approaches using tumor associated antigens or vaccines in order to enhance immunogenicity.

e. Develop and characterize novel chemical compounds that may be useful anticancer agents, either alone or in combination with other modalities such as radiotherapy.

f. Develop techniques to lessen the toxicity of existing anticancer treatments.

g. Develop new techniques for the delivery of anticancer agents that will maximize therapeutic effects and minimize toxicity.

h. Develop new surgical techniques or tools or improve existing techniques that are/may be utilized in cancer treatment.

i. Characterize and produce clinical grade monoclonal antibodies to detect and treat malignancies.

2. *Development of Prognostic Assays to Monitor Patient Response to Therapies*.

a. Develop assay systems to measure the response of human tumors to chemotherapy or biologics.

b. Characterize drug resistance mechanisms and design methods to overcome clinical drug resistance.

c. Develop assays for prognostic factors to identify patient subsets who may benefit from specific cancer treatment therapies.

d. Development of assays to assess effects of agents on specific molecular targets in clinical studies.

e. Develop new techniques for relating past preclinical information to past clinical results for prediction of future useful clinical agents from future preclinical data (both in vitro and in vivo).

3. *Clinical Trials Informatics*.

a. Develop new tools and methodologies for the analysis of clinical trials results.

b. Develop new informatics tools to facilitate clinical trials data entry from the bedside and coordination of data entry and transmission throughout the institution and to other collaborating institutions or organizations.

c. Development of novel web-based approaches to clinical trials informatics for transmission of data to NCI or other organizations. Topics include point of treatment data capture and reporting, electronic protocols, OLAP (On-line Analytical Processing), support for the Common Toxicity Criteria, and drug accountability support.

d. Develop new interchange standards, based on technologies such as XML, for sharing data among heterogeneous systems. Specific applications areas include, Adverse Even Reporting, Case Report Forms.

e. Develop new tools for support of Common Data Elements.

f. Develop new approaches for interface with electronic medical records, with intent to streamline data reporting, registration, and toxicity reporting of Clinical Trial information.

E. ***Cancer Imaging Program.*** The mission of this program is to promote and support: Cancer-related basic, translational and clinical research in imaging sciences and technology, and integration and application of these imaging discoveries and developments to the understanding of cancer biology and to the clinical management of cancer and cancer risk.

Toward this effort, CIP 1) funds research in the development of tools, methodologies and imaging agents/probes that will better diagnose, assess, and effectively treat cancer, and 2) supports a spectrum of research projects from preclinical exploratory research and development through clinical trials. Specifically:

1. Development of medical imaging systems for early cancer detection, screening, response to therapy and interventions including image-guided therapy.

2. Development of preclinical and clinical in vivo imaging systems, methods, imaging probes and contrast agents and related image reconstruction, image processing, image display and image-based information as required to detect, classify, monitor and guide therapeutics to cancer and precancerous conditions.

3. Development of methods to assess the value of imaging procedures for the above goals.
4. Development of systems and methods for improved production and distribution of radioactive materials for cancer imaging and/or treatment.
5. Development of systems, methods and their optimization for studying the adverse reactions/effects of image-guided and other diagnostic and therapeutic interventions.
6. Any other investigator-initiated research idea that is relevant to cancer biomedical imaging.
7. Development of systems, methods and their optimization to advance the role of imaging in assessment of response to therapy through increased application of quantitative anatomic, functional, and molecular imaging endpoints in clinical therapeutic trials and dissemination of these systems and methods with appropriate scientific communities.

F. ***Radiation Research.*** The Radiation Research Program (RRP) supports basic, developmental and applied research (including clinical) related to cancer treatment utilizing ionizing and non-ionizing radiations. Therapeutic modalities include photon therapy, particle therapy, photodynamic therapy (PDT), hyperthermia, radioimmunotherapy (RIT), systemic targeted radionuclide therapy (STaRT), and boron neutron capture therapy (BNCT). Radiation research encompasses a range of scientific disciplines including basic biology, chemistry, physics and clinical radiation oncology. Topics of interest include, but are not limited to, the following areas:

1. Development of devices for planning, measuring, and delivering radiation therapy or related therapies, including devices for patient positioning and quality assurance for the following: (a) ionizing radiation, particularly 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT); (b) PDT; (c) hyperthermia; (d) RIT; (e) STaRT; and (f) particle therapy.
2. Development of devices for dosimetry for (a) ionizing radiation; (b) PDT, particularly those capable of measuring light doses at depth in tissues; (c) thermometry for hyperthermia, particularly non-invasive thermometry; and (d) RIT.

   Devices may include chemical, solid state, film, biological or ionization systems to detect or read out exposures. Accuracy, precision and linear response are essential over the range of doses and temperatures employed in the research laboratory and/or in the clinic, depending on their intended use. Devices for thermometry during hyperthermia treatment must give accurate readings with the heating device(s) with which they are to be used.
3. Development and evaluation of computer hardware and software for radiation therapy, such as computation algorithms, computer workstations, image guidance techniques, and informatics methods for treatment planning, delivery and outcomes analysis.
4. Development of novel drugs to increase the effectiveness of radiation therapy or related therapies: (a) chemical modifiers of radiation response, particularly small molecules directed at molecular targets involved in tumor radioresistance; (b) photosensitizers for PDT; (c) sensitizers for use with hyperthermia; and (d) prodrugs that are selectively activated within the tumor.
5. Development of drugs to prevent, reduce or reverse normal tissue response, especially the late effects that develop months or years after therapy.

   Compounds that are based on a rationale for achieving a therapeutic gain (an improved differential response between tumor and normal tissue) are of greatest interest. Enhancement of response must be achieved at radiation doses and treatment schedules employed clinically.
6. Development of predictive assays and monitors of response to radiotherapy, PDT, hyperthermia, STaRT, or RIT. Tools are needed to identify patients that would benefit from specific therapeutic approaches.

G. ***Biological Response Modifiers (BRM).*** Research on agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells with resultant therapeutic benefits.

Both preclinical and clinical investigations are conducted on the utility of a wide variety of natural and synthetic agents and on biological manipulations of immunological and non-immunological host mediated, tumor-growth controlling mechanisms in cancer therapy.

Studies are encouraged which utilize in vitro assays and/or animal model systems to investigate mechanisms of BRMs. Examples of innovative research that would be responsive to this solicitation include:

1. Evaluation of molecular genetic approaches to discovery of new therapeutic agents, delivery of BRMs or development of gene therapy.
2. Development of improved techniques to synthesize, screen and develop new oligonucleotides including iRNA sequences for therapeutic purposes, such as signal modulation, anti-ongogene or anti-viral effects.
3. Improvement in cell-culturing techniques, e.g., by developing automated cell culture systems, specialized media, or improved methods to induce activation, proliferation or differentiation.
4. Development of new procedures or reagents for the modulation of the suppressor arm of the immune system in experimental models, directed towards successful immunotherapy.
5. Improvement of tumor-associated antigens or vaccines in an attempt to enhance immunogenicity.
6. Evaluating autoimmunity in the context of anti-tumor response *in vivo* to vaccines.
7. Development of novel in vitro assays for the primary screening of BRMs.
8. Application of observations describing shared receptors and mediators between the neuroendocrine and immune systems in studying immunobiology and immunotherapy of cancer.
9. Development and optimization of viral oncolytic agents.
10. Development of novel or improved methods for process development and manufacture of biotherapeutics, including but not limited to antibodies, recombinant proteins, peptides, oligonucleotides, and products based on viral or bacterial vectors, per executive order (E.O. 13329) mandating federal agencies assist the private sector in manufacturing innovation efforts.
11. Development of innovative methods for monitoring the manufacturing process for biotherapeutics using in-line or on-line process analyzers to improve the efficiency of process controls and determination of production end-points (see Guidance for Industry, PAT-A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance, www.FDA.gov).
12. Development of methods to more efficiently assess factors related to the ultimate product quality, safety and efficacy of biologics.

Division of Cancer Prevention

The Division of Cancer Prevention (DCP) directs an extramural program of cancer prevention research including chemoprevention, nutritional science, genetic, epigenetic, and infectious agent, early detection including biomarker development and validation and biometry for the Institute. DCP also supports research training and career development in cancer prevention and early detection and coordinates community-based clinical research in cancer prevention and dissemination of cancer treatment practice through a consortium of community clinical centers. For additional information, please visit our home page at http://dcp.nci.nih.gov/.

A. ***Prevention.*** Research studies to identify, evaluate, and implement techniques and approaches for the prevention, risk assessment, and early detection of cancer. Those studies capable of achieving these objectives with minimal risk and cost are preferred.

   1. *Chemoprevention*. Studies in which naturally occurring or synthetic agents are identified, or further evaluated for efficacy or safety. Studies involving in vitro assays with cell transformation systems, in vivo assays involving animals models to evaluate agents against typical carcinogenic agents at specific sites, and studies involving clinical chemistry measurement of agents in sera or other biological fluids are of highest program relevance. Studies aimed at improving

future research designs for chemopreventive trials; providing additional biological understanding, identification and evaluation of modulation of quantitative or qualitative biological endpoints, and/or markers for surveillance of compliance will also be considered. Examples of tests might include measurements of biochemical parameters, cytological screening techniques, in vitro studies of suppression of oncogene protein products, enhancement of tumor suppressor genes, in vitro toxicological studies, and synthesis of novel chemopreventive agents based on structure/activity relationships.

2. *Diet and Nutrition*. The Nutritional Science Research Group supports studies that aim to reduce the incidence of cancer through dietary modification, which may include additions, deletions, or substitutions of foods or dietary factors.

   Topics of interest include:

   a) In vivo animal models, including transgenics and knockouts, to examine the cancer prevention effects of essential and non-essential nutrients.

   b) Invertebrate models for the study of bioactive food component-gene interactions involved with cancer prevention.

   c) Novel technologies for measuring the effects of diet on differential gene expression, epigenetic events, proteomics, and associated metabolomic changes.

   d) New models/approaches for examining diet-immunity interactions.

   e) Educational interactive software packages that focus on dietary exposures and cancer prevention.

   f) New and improved diagnostic markers for nutritional status.

   g) New methods to detect and identify anticarcinogenic nutrients in foods.

   h) New methods for the isolation and preparation or synthesis of candidate nutrients in quantities suitable for preclinical and clinical screening.

   i) Valid, more facile and effective methods for assessing the content of bioactive food components in foods and dietary supplements.

   j) Transgenic/knockout food models for testing the physiological significance of bioactive food components within the food matrix.

   k) Combinations or blends of bioactive food components for cancer prevention, including the importance of the food matrix.

   l) Bioinformatics tools for the study of bioactive food components as regulators and modulators of genes associated with cancer prevention.

   m) New bioengineering tools for the study of bioenergetics and obesity.

B. ***Community Oncology.*** Introduction, application, and evaluation of effective and practical cancer control intervention programs in community settings. Primary emphasis is on the integration and involvement of community physicians and allied health professionals in cancer control efforts and the promotion of linkages between community practitioners/hospitals and other regional resources for cancer control.

   Objectives are to: (1) reduce the time between research advances in prevention, detection, and patient management and their application in community settings; and (2) expand extend the cancer care knowledge and applications bases; and (3) evaluate new detection and diagnostic methods for specificity, sensitivity, reliability, validity, safety, feasibility and cost when applied to defined or target populations. This may include screening research as well.

C. ***Rehabilitation and Continuing Care.*** Development and evaluation of rehabilitation or continuing care strategies which directly enhance functioning of patients with cancer or which contribute to understanding of factors impacting utilization of supportive services by cancer patients. Clinical applications include development and testing of interventions to enhance multidisciplinary approaches to cancer rehabilitation, and research on effective symptom management (e.g., cancer-related pain, fatigue, nausea, mucositis). Areas of general program interest include innovative approaches to measuring and enhancing quality of life of cancer patients; research to investigate and enhance clinical decision-

making by both patients and physicians; and studies of the impact of individual preferences for health care outcomes and their impact on cancer prevention practices in persons without cancer and on treatment decisions in patients with cancer.

D. ***Early Detection and Screening.*** New diagnostic or screening methods for early detection of cancer, especially for asymptomatic patients. Detection methods can include any cancer site, although there is more interest in the common cancers, such as those of the lung and colon. Methods should be cost beneficial and applicable in a clinical setting.

1. Studies which identify and document new databases relevant to early cancer detection and propose using new and experimental analytical techniques.
2. Analyses of long-term, follow-up data from completed studies for potential new interpretations based on the passage of time.
3. Studies which propose to develop and evaluate new detection techniques and measures for sensitivity specificity, reliability, validity and safety.
4. Determinations of the cost/benefit or risk/benefit ratios of cancer screening and detection methods when applied in defined or target populations.
5. Currently, the most commonly used method to detect prostatic cancer is the digital rectal examination. Various devices and models would be necessary for the early detection of prostate cancers by physical examination. They would include, but not limited to the following disease states: (1) absence of disease (normal model); (2) benign prostatic hypertrophy; (3) prostatitis; (4) Stage B1 prostatic cancer (T2a); (5) Stage B2 prostatic cancer (T2b); and (6) Stage C prostatic cancer (T3z, T3b, and T4).
6. Development of products that aid the systematic collection and transport of specimens used for the early detection of cancer, including devices for the collection and transport of urine, serum, fecal material, exfoliated cells, and other potential materials.
7. Develop computer utility programs that can increase the clinical uses of existing programs commonly found in medical offices creating age-sex registries, predicting population risks, determining screening needs of patients, reminder systems, etc. Develop bioinformatics to study gene profiling.
8. Develop personal computer programs that can be used to determine population risks and the effect of interventions. These programs might also be adopted to the concept of Community Oriented Primary Care.
9. Use of ultrasonography with color flow imaging for the early detection of cancer. Research on the use of ultrasonography with color flow imaging (US-CFI) for the early detection of cancer of the ovary, breast and/or prostate. Emphasis should be given to the ability of the US-CFI to differentiate between malignant and benign disease at these sites. Criteria for the discrimination of malignant from benign disease would be developed as well as performance characteristics of this method, particularly for breast and prostate. Studies on symptomatic populations should yield sensitivity, specificity and positive predicative values when breast and prostate are the target sites. Studies on asymptomatic populations should yield sensitivity, specificity and positive predicative values when ovarian cancer is the target site.
10. As more women seek mammographic breast screening, the importance of efficient, high speed, “intelligent” mammographic systems capable of acquiring and storing large volumes of images and enhancing image interpretation will become more important. Technological developments of interest are:
    a. Develop digital mammographic systems for high volume applications with electronic archiving and image analysis capabilities.
    b. Develop artificial intelligence based interactive image analysis software to enhance mammographic sensitivity and specificity.

E. ***Cancer Biomarkers.*** The Cancer Biomarkers Research Group (CBRG) promotes research on the discovery, development, and validation of biomarkers for pre-cancer and early cancer detection and relevant technologies so that risk can be more accurately assessed and cancers can be detected at early stages of development. Early detection has the potential to reduce cancer morbidity and mortality. In cancer research, biomarkers refer to substances that are indicative of the presence of cancer in the body. Biomarkers include genes, RNAs, proteins, and metabolites. As the molecular changes that occur during tumor development can take place over a number of years, biomarkers can be potentially used to detect cancers early. Topics of interest include, but are not limited to, the following areas:

1. Discovery, development and/or validation of biomarkers (genomic, epigenomic, proteomic and metabolomic) for precancerous lesions, early cancer detection, and identification of risk.
2. Development of new biological, genetic, histochemical, immunologic, and molecular assay or analyses applied to early cancer detection, risk assessment, or susceptibility.
3. Development of new tools and technologies, including microfluidics and nanotechnologies, for analyzing biomarkers for early cancer detection and risk assessment.
4. In silico data analysis for the discovery and identification of cancer biomarkers.
5. Ancillary studies to discover biomarkers from ongoing prevention and treatment trials and any large studies.
6. Development of statistical and epidemiological approaches to biomarkers evaluation for early cancer detection and risk.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Mr. Michael Weingartenr
National Cancer Institute
31 Center Drive, MSC 2580
Room 10A52
Bethesda, MD 20892
(301) 496-1550
Email: weingartenm@mail.nih.gov

Website: http://otir.nci.nih.gov/smallbusiness/small_sbir.html

CENTER TO REDUCE CANCER HEALTH DISPARITIES
HTTP://CRCHD.NCI.NIH.GOV/

Dr. Emmanuel A. Taylor
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DIVISION OF CANCER BIOLOGY
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DIVISION OF CANCER CONTROL AND POPULATION SCIENCES
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Cancer Epidemiology and Genetics
http://epi.grants.cancer.gov/
Mr. Jay Choudhry
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6130 Executive Boulevard, Room 5109
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Multimedia Technology and Health Communication in Cancer Control
http://cancercontrol.cancer.gov/hcirb/sbir/
Ms. Connie Dresser
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6130 Executive Boulevard, Room 4072
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DIVISION OF CANCER TREATMENT AND DIAGNOSIS
HTTP://CANCER.GOV/DCTD/

Cancer Diagnosis Program
http://www.cancerdiagnosis.nci.nih.gov/

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Cancer Therapy Evaluation Program
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Cancer Imaging Program
http://cip.cancer.gov/
Dr. Keyvan Farahanil
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6130 Executive Boulevard, Room EPN 3006
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Radiation Research Program
http://www3.cancer.gov/rrp/
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(301) 496-9360, Fax: (301) 480-5785
Email: stoneh@exchange.nih.gov

Biological Response Modifiers
http://web.ncifcrf.gov/
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P. O. Box B Building 1052 Room 253
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DIVISION OF CANCER PREVENTION
HTTP://WWW.CANCER.GOV/PREVENTION/

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Nutritional Science Research Group
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Email: rosssha@mail.nih.gov

For administrative and business management questions, contact:

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For NCI-related SBIR Information, visit:
http://www3.cancer.gov/admin/gab/index.htm

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

The NICHD conducts and supports research and research training on biological and behavioral aspects of human development. Primary program areas include: reproduction and population studies, pregnancy, perinatal biology, maternal and infant well-being, developmental and reproductive immunology, congenital defects, developmental biology, teratology, nutrition and growth, human learning and behavior, learning disabilities, cognitive and social development, mental retardation and developmental disabilities, pediatric, adolescent, and maternal AIDS and HIV, obstetric and pediatric pharmacology, and medical rehabilitation.

For additional information about areas of interest to the NICHD, please visit our home page at http://www.nichd.nih.gov.

Phase II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-029.html STTR and http://grants.nih.gov/grants/guide/pa-files/PA-06-030.html SBIR.)

NICHD will accept Phase II SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Applicants who received either NICHD SBIR/STTR Phase I or Phase II support and who are currently Phase II awardees are eligible.

You are strongly encouraged to contact Dr. Louis Quatrano (contact information provided below) before beginning the process of putting a Phase II Competing Renewal application together. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NICHD SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities. Preclinical studies, including pharmacology and toxicology, and other clinical studies beyond those conducted under the initial Phase II (R42, R44) grants such as:

- innovative assistive devices and techniques to minimize residual disability and to impact on critical illness, physical behavior and cognitive development in childhood;
- novel assays, kits, and devices to monitor fertility;
- new and improved methods of fertility regulation, for men and for women, that are safe, effective, inexpensive, reversible, and acceptable;
- new tools to monitor the state of various organ systems during therapy in pregnancy or infancy; and,
- Evaluation of neuroimaging tools specific to brain development in pediatric populations or individuals with injuries.

Direct your questions about scientific/research issues to:

Louis A. Quatrano, Ph.D.
National Institute of Child Health and Human Development
(301) 402-4221, Fax: (301) 402-0832
Email: lq2n@nih.gov

Population Research

Research on topics in reproductive sciences, contraceptive development, and demographic and behavioral sciences. Examples of research topics that may be of interest to small businesses include, but are not limited to:

A. ***Reproductive Sciences.*** Research on the reproductive processes of men and women and of animals with similar reproductive systems related to developing safer and more effective means of regulating, preserving or achieving fertility. Particular areas of programmatic interest relative to small business initiatives include, but are not limited to:

1. Development of reagents to facilitate study of reproductive and developmental processes.
2. Development of improved methods of growing and differentiating stem cell lines in vitro, including feeder cell-free approaches.
3. Development of novel assays, kits, and devices to monitor fertility and treat infertility and gynecological disorders.

4. Use of genomics and proteomics to develop novel diagnostics and treatments for reproductive diseases and disorders.
5. Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
6. Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.
7. Development of improved and novel technologies for the preservation of human gametes.
8. Development of improved technologies for preimplantation genetic diagnosis.
9. Development of improved technologies for the reprogramming of cells, including embryonic stem cells or adult cells, into eggs and sperm.

Dr. Susan Taymans
(301) 496-6517, Fax: (301) 496-0962
Email: taymanss@mail.nih.gov

B. ***Contraception and Reproductive Health Research.*** Emphasis is on developing new and improved methods of fertility regulation; developing new and improved treatments for disorders of the reproductive system including female pelvic floor disorders; and research on the benefits and risks of contraceptives and other drugs, devices, and surgical procedures as they affect reproductive health. Areas of interest include, but are not limited to:

1. Developing new and improved methods of fertility regulation, for men and for women that are safe, effective, inexpensive, reversible, and acceptable. This includes, but is not limited to, synthesis and testing of novel chemical compounds.
2. Developing new and improved treatments for disorders of the male and female reproductive system, including those used for hormone therapy and drugs, graft materials, and devices used for non-surgical and surgical treatment of pelvic organ prolapse, urinary incontinence, and other female pelvic floor disorders.
3. Discovering and disseminating new knowledge about the medical benefits and risks of contraceptives and other drugs, devices, and surgical procedures affecting reproductive health. We will primarily support applied research projects such as epidemiologic studies or Phase III/IV trials designed to detect clinically significant adverse effects, particularly those too rare to be determined through the FDA's premarketing approval process. Laboratory models will be used when human studies are not feasible or to explore mechanisms of action or supplement epidemiologic and clinical observations.
4. Studies relating contraception or reproductive health to STDs such as HIV, including but not limited to development of new products with microbicidal activity against STDs such as HIV; studies to define the relationships among contraceptive methods and HIV acquisition, transmission, or disease progression; development of diagnostic and other research models for HIV and contraception/reproductive science; and studies to clarify mechanism of interaction between contraceptives and other disease processes or conditions.

Dr. Steven Kaufman
(301) 435-6989, Fax: (301) 480-1972
Email: sck@nih.gov

C. ***Demographic and Behavioral Sciences.*** Research on the size, growth, and composition of populations and the impact of changes in population on the health and well-being of individuals, families, and the population itself. The program emphasizes not only factors affecting fertility, mortality, population movement and compositional change, but also teenage childbearing, AIDS, single-parent families, racial and ethnic differentials in infant mortality, legal and undocumented immigration, and the well-being of children. Applications are encouraged in these areas:

1. Innovative use of geographical information systems and spatial network analysis.
2. Innovative approaches to analyzing and disseminating large-scale data sets.
3. Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, and other mission-related topics.

4. Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.
5. Innovative approaches for research design, data collection techniques, measurement, and data analysis techniques in the social and behavioral sciences, with particular attention to methodology and measurement issues in studying diverse populations, sensitive behaviors, confidential behaviors; in issues related to the protection of research subjects; and in issues related to the archiving and disseminating complex datasets.

Dr. Rebecca L. Clark
(301) 496-1175, Fax: (301) 496-0962
Email: rclark@mail.nih.gov

Research for Mothers and Children

Research in three major program areas includes: learning disabilities; cognitive and social development; nutrition and growth; obstetric and pediatric pharmacology, and pediatric, adolescent, and maternal AIDS. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

A. ***Child Development and Behavior.*** Research and research training programs in developmental psychology (cognitive, affective, and social development), cognitive psychology, cognitive neuroscience, language acquisition and bilingualism, developmental neuropsychology, behavioral pediatrics, and educational psychology; studies to define, classify, and map the developmental course of specific learning disabilities and disorders of attention; studies to elucidate the etiological role of cognitive, linguistic, perceptual, educational, genetic, social, and neurobiological mechanisms in dyslexia, mathematical disabilities, learning disabilities, language disorders, and disorders of attention; investigations of the effects of well-defined treatment interventions on specific types of learning disabilities; studies designed to understand the development of attention, reasoning, planning, problem solving, and concept formation in children; basic and intervention research in mathematics and science cognition and learning; studies delineating the effects of motivation, emotion, societal, cultural, familial, and neurobiological influences on social, emotional, and cognitive development; examinations of the effects of parental and non-parental care on social, emotional, and cognitive developmental outcomes; and investigations of temperament, motivation, self-concept, attitudes, and values, and their relationship to development. Research and development of neuroimaging tools specific to brain development in pediatric populations, including research or tool development using EEG, magnetic resonance imaging (MRI), functional MRI, magnetic spectroscopy (MRS), diffusion tensor imaging (DTI), and near infrared spectroscopy. Biobehavioral research on preventive measures for injuries and risk behaviors (alcohol, tobacco, other illicit drug use, sexual risk behaviors, gambling, suicide, and antisocial behavior). The development of training programs (CD-ROM, website, etc.) and research designed to promote health (physical activity, spirituality, adherence to medical and therapeutic regimens, and mind-body) and prevent diseases and unhealthy conditions (HIV, sexually transmitted diseases, obesity, eating disorders, pain, stress, and sleep disorders). Research and development projects on assessments tools for use in child outcomes assessment, processes of interaction between children and parents and other caregivers, and tools for use in measuring environmental and other contextual factors in development, and the application of technology to aid in conducting these assessments.

Dr. Reid Lyon
(301) 496-9849, Fax: (301) 480-0230
Email: rl60a@nih.gov

B. ***Endocrinology, Nutrition, and Growth.*** Research on the nutritional needs of pregnant women and their fetuses; aspects of nutrients related to reproduction, growth, and development; breast feeding and lactation; the immunology of breast milk; development of the gastrointestinal system; childhood obesity and the nutritional antecedents of adult disease; developmental endocrinology; mechanisms of hormone action during growth and development, and the impact of hormonally active agents in the environment on growth and development. Applications to advance the study of obstetric and pediatric pharmacology include: Research and tools to better characterize the impact of physiological and developmental changes on pharmacokinetics

and pharmacodynamics; advancements in modeling which improve therapy during pregnancy, among premature infants, children and adolescents; research on tools to monitor the state of various organ systems during therapy in pregnancy or infancy; such as, cerebral monitors, placental function, etc.; models to characterize molecular, dosing or other modification to improve therapy.

Dr. Gilman D. Grave
(301) 496-5593, Fax: (301) 480-9791
Email: gg37v@nih.gov

C. ***Pediatric, Adolescent, and Maternal AIDS.*** Research on all aspects of HIV (human immunodeficiency virus) infection and disease, including AIDS in women of child-bearing age, pregnant women, mothers, fetuses, infants, children, and adolescents. Areas of interest include, but are not limited to, epidemiology, natural history, pathogenesis, treatment, and prevention.

Dr. Robert Nugent
(301) 435-6871, Fax: (301) 496-8678
Email: rn22e@nih.gov

Developmental Biology & Perinatal Medicine Research

Research in three major program areas includes: pregnancy and Perinatology; developmental biology, genetics and teratology; and mental retardation and developmental disabilities. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

A. ***Pregnancy and Perinatology.*** Research on the physiology of pregnancy and labor; high-risk pregnancies, including those with hypertensive disorders, diabetes or seizure disorders; fetal pathophysiology; premature labor and birth; diagnostic, monitoring, and therapeutic devices and instruments for newborn infants in the nursery and in Neonatal ICU setting; improving the existing products or developing new products that would improve the routine and extended care of the newborn infants; products and agents related to breastfeeding; hospital supplies specifically related to use in the care of newborn infants; nanotechnology and its application for the care of newborn infants; instruments and devices assessing and monitoring the nursery environment (noise, lighting, and odor); disorders of the newborn; sudden infant death syndrome; and biological and behavioral antecedents of low birth weight.

Dr. Tonse Raju
(301) 496-5575, Fax: (301) 496-3790
Email: rajut@mail.nih.gov

B. ***Development Biology, Genetics, and Teratology.*** Biomedical research on the cellular, molecular, and genetic aspects of normal and abnormal embryonic and fetal development and its aberrations, including early embryogenesis, limb formation, development of the nervous system, developmental and reproductive immunology, and causative factors in teratogenesis. Applications to develop and apply new animal model systems or innovative and high throughput genomic and proteomic technologies to advance the study of embryonic development, structural birth defects, and newborn screening are particularly welcome.

Dr. Lorette Javois
(301) 496-5541, Fax: (301) 480-0303
Email: lj89j@nih.gov

C. ***Mental Retardation and Developmental Disabilities.*** Biomedical research in neuroscience, genetics, biochemistry, molecular biology, and psychobiology aimed at identifying factors that cause abnormal brain maturation and function; identification of direct and indirect social, economic and cultural influences on the occurrence of mental retardation and developmental disabilities (MRDD); and research leading to the assessment, prevention, and amelioration of MRDD, including screening and prenatal diagnosis.

Dr. Mary Lou Oster-Granite
(301) 496-1383, Fax: (301) 496-3791
Email: mo96o@nih.gov

Medical Rehabilitation Research

This Center supports innovative research on the restoration, replacement, enhancement or adaptation of function for people with chronic physical disabilities. This includes rehabilitative approaches across etiologies and the lifespan, as well as the environmental and policy factors that promote full participation. We encourage studies that integrate biomedical, engineering and/or psychosocial approaches to develop practical and creative solutions to the daily functioning of people

with disabilities and their families. The mission of the NCMRR is to increase the effectiveness of medical rehabilitation practices through research. Information about specific program areas within NCMRR can be found at: http://www.nichd.nih.gov/about/ncmrr/ncmrr.htm. Examples may include:

A. Improving functional mobility.

B. Promoting behavioral adaptation to functional losses.

C. Assessing the efficacy and outcomes of medical rehabilitation therapies and practices.

D. Developing improved assistive technology.

E. Promoting rehabilitative outcomes in pediatric critical care.

F. Understanding whole body system responses to physical impairments and functional changes.

G. Developing more precise methods to measure impairments, disabilities, and societal limitations.

H. Training health professionals in the field of medical rehabilitation.

I. Enabling technologies for restoration of function.

J. Promoting profession structured/directed self care and wellness.

Investigators proposing budgets exceeding the guidelines should contact program six weeks prior to submitting the application. Study section approval of projects exceeding the guidelines may not be supported at the level requested.

For additional information on research topics, contact:

Nancy Shinowara, Ph.D.
(301) 495-6838, Fax: (302) 402-0832
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or

Dr. Louis A. Quatrano
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Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

The mission of the NIDA is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy. For additional information about areas of interest to the NIDA, please visit our home page at http://www.nida.nih.gov/.

Phase II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-036.html SBIR)

NIDA will accept Phase II SBIR Competing Renewal grant applications to continue the process of developing products that require approval of a Federal regulatory agency. Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Please contact Dr. Cathrine Sasek (contact information provided below) before beginning the process of putting an application together. Prospective applicants are also strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator

- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIDA SBIR Phase II awards will be eligible for a Competing Renewal grant.

The following examples would make appropriate topics for proposed SBIR Phase II Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities.

Research and development efforts can be focused on medications for the treatment of cocaine, methamphetamine, and other stimulant abuse, as well as towards opiate, cannabis, PCP and club drugs. The medications under development should be targeted towards attainment of abstinence, maintenance, and/or relapse prevention.

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development of the entity or entities.
- Completion of studies as required by the FDA for an IND application.
- Human laboratory clinical trials to determine a medication's safety profile, metabolism, cardiovascular effects, interaction with drugs of abuse, etc.
- Clinical studies to assess the efficacy of the medication under development.

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Division of Pharmacotherapies & Medical Consequences of Drug Abuse

The NIDA Division of Pharmacotherapies & Medical Consequences of Drug Abuse (DPMCDA) supports research aimed at the development and testing of pharmacological and behavioral treatments for drug abuse and addiction. This includes the identification, evaluation, development, approvability, and efficacy testing of new and improved pharmacotherapeutic agents, as well as the testing of marketed medications, and of behavioral treatments used alone or integrated with medications. The DPMCDA also advances a human neuroscience research and training program focused on understanding the neurobiological substrates of drug abuse and addiction processes.

A. ***Chemistry and Pharmaceutics Branch (CPB).*** The CPB supports research in the design (including molecular modeling and structure-activity relationship studies) and synthesis of novel compounds, formulation development, bioanalytical methods development, and pharmacokinetics/ pharmacodynamics aimed at the discovery and development of new medications for treating drug addiction. Areas that may be of interest to small businesses include, but are not limited to *research related to the design and development of new compounds and improved drug products (drug delivery) for the treatment of drug addiction*:

1. Synthesis (either using traditional or combinatorial techniques) or discovery (natural products) of new chemical compounds that would have potential as treatment agents for the medical management of stimulant (e.g., cocaine, methamphetamine, or nicotine) addiction. Consideration should be given to the design of partial agonists or pure antagonists that diminish the reinforcing effects of stimulants, as well as full agonists that could function to normalize physiological activity following discontinuation of stimulant use.

   Compounds of interest include those that are designed to affect dopaminergic (i.e., D1 agonists, D3 agonists and D3 antagonists) activity, CRF antagonists, compounds affecting glutamate activity, GABAergic activity, small molecule neuropeptide antagonists and compounds

acting through other mechanisms for which justification has been supplied.

2. Synthesis (either using traditional or combinatorial techniques) of new chemical compounds that would have potential as treatment agents for the medical management of cannabinoid abuse.
3. Development of new immunotherapeutic treatments that would have the potential as treatment agents for stimulant, opioid or cannabinoid abuse.

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4. Development of new approaches for the administration of potential addiction treatment drugs with poor bioavailability.
5. Development of controlled release dosage forms for addiction treatment medications in order to maintain therapeutic drug levels for extended periods of time to alleviate compliance problems associated with addiction treatment.

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B. ***Medications Discovery and Toxicology Branch (MDTB).*** The MDTB supports research on the development of preclinical behavioral models (e.g., of craving, drug-seeking behavior, dependence, or relapse), biochemical assays, gene expressional assays and electrophysiological methods to identify and characterize new medications to treat substance abuse, as well as pharmacological screening of novel compounds to identify potential drug abuse medications. The Branch also supports research on toxicity studies of potential medications for the treatment of substance abuse, and interactions of potential treatment medications with abused substances. Areas that may be of interest to small businesses include, but are not limited to *development of new methods for discovery of medications useful in treating drug addiction*. Of special interest would be the development of new animal models of addiction, incorporating established drug self-administration techniques that show increased relevance to the clinical setting. Development of relevant biochemical or electrophysiological screening methods is also encouraged.

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C. ***Medications Research Grants Branch (MRGB).*** The MRGB supports investigations of the use of therapeutic agents (including vaccines and monoclonal antibodies) for the treatment of substance related disorders, with the aim of assisting in reducing drug use, becoming drug free, prolonging abstinence, decreasing associated psychosocial, medical or legal problems, or surviving drug overdose. In general, therapeutic agents are expected to be investigated using a platform of appropriate psychosocial interventions. The program funds extramural grants in the following:

- Clinical trials to test the safety, find the optimal dose, and/or obtain preliminary efficacy data for new agents or new indications of marketed medications. This phase includes interaction studies to test the safety of the agent when used in combination with drugs of abuse.
- Clinical trials to assess the efficacy of new agents or marketed medications for the treatment of substance related disorders. In general, these types of trials use a randomized double blind placebo controlled design.
- Clinical studies of the efficacy of medications for the treatment of the comorbidity of substance related disorders (e.g., alcohol and cocaine dependence) or the comorbidity of these disorders with other medical or psychiatric conditions.
- Clinical evaluation of the efficacy of medications for the treatment of substance related disorders in specific groups of the population. For example, adolescents, the elderly, women of childbearing age, pregnant and/or postpartum women, as well as racial and ethnic minorities.
- Evaluation of biological and/or psychosocial factors that may affect the outcome of the pharmacotherapy of substance related disorders.

Specific areas that may be of interest to small businesses include, but are not limited to:

1. *Pharmacogenetics and Substance Use Disorders (SUD).* The emergence of new genetic techniques may allow the use of genetic information to improve the safety and efficacy of treatments. The field of pharmacogenetics focuses on the genetic determinants of response to medications and other therapies in humans and animals. The goal is to discover novel single nucleotide polymorphisms (SNPs) and test their relevance to the underlying genetic differences that determine the safety and efficacy of medications for the treatment of SUD. It includes the study of genes encoding drug metabolizing enzymes, transporters, receptors and other drug targets, polygenic determinants of drug disposition and effects in humans, the role of genes in the clinical response to and medical safety of medications, and application of genetic information to disease prevention and to optimize treatments in humans. It also includes novel methods for phenotyping the diagnosis, safety and treatment outcome of SUD. Ultimately, it is expected that pharmacogenetics research will help clinicians to individualize the treatment of their patients based on their genetic information. Research is needed to study the genetic factors that may be associated with drug abuse treatment safety and outcome.

2. *Medications Development for the Treatment of Drug Abuse in Adolescents.* Drug abuse among adolescents is a significant and growing public health concern. It is known that the pharmacokinetics and pharmacodynamics of some medications are different in adolescents. Therefore, adolescents may present overdoses, underdoses or lack of efficacy, or different safety profiles when administered medications at the doses studied only in adults. Unfortunately, little is known about the safety and efficacy of medications for the treatment of drug abusing adolescents because most of the drug abuse medication research has focused on adults. Research is needed to test medications for the treatment of nicotine and drug abuse in adolescents.

3. *Medications for the Treatment of Pregnant and Post-Partum Drug Abusing Women and Their Children.* Little is known about the safety and efficacy of medications for the treatment of substance abusing pregnant women and their children. There is a need for safe and effective medications for the treatment of nicotine and drug abuse/dependence among pregnant and post-partum women and the effect of these medications on their children. Research is also needed to study the effects on the newborn of the medications taken by the mother and medications for treatment of children born to substance abusing mothers who may present drug withdrawal and other symptoms.

4. *Medications for the Treatment of Comorbid Medical or Mental Disorders and Drug Abuse.* Co-morbid medical and psychiatric conditions are frequently found among substance abusing patients. Co-occurring mental disorders, such as depression, post-traumatic stress disorder, and anxiety disorder, and medical conditions such as hepatitis C, AIDS related disorders, and pain, are common among substance abusing patients. Unfortunately, there are presently no commonly prescribed safe and effective medications for the treatment of substance abusing patients with other co-morbid medical and psychiatric conditions. Research is needed to study the safety and therapeutic profiles of medications for treatment of substance abuse in patients with other comorbidities. There is also a need to study the effects of medications for the treatment of substance use disorders in patients taking medications for other comorbid conditions and the necessary dose adjustments.

5. *Development of Software and/or Other Tools for Data Collection and Statistical Analysis of Clinical Trials Testing the Safety and Efficacy of Therapeutic Agents for the Treatment of Substance Related Disorders.* Current data collection techniques often have questionable validity and reliability and statistical data analysis pose particular challenges. They range from lack of well defined outcome measures to having a large amount of missing data, which may be due intermittent missing data points to early

subject drop out (attrition). To solve those challenges, investigators have developed pragmatic methods to analyze their data. For example, carry forward data from the last timepoint, data replacement by regression, end point analysis by regression, or worst case scenario, they all have important statistical limitations. The purpose of this initiative is to stimulate research on innovative data management tools to improve data collection and analysis of data from nicotine and drug abuse clinical trials.

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6. *Immunotherapy for Addiction Treatment.* The MRGB supports research on the advanced stage development of monoclonal antibodies and vaccines for the treatment of drug and nicotine addiction and/or overdose. Monoclonal antibodies have been reported as possible treatment agents through passive immunization for PCP, methamphetamine, MDMA, and cocaine overdose and may also serve to minimize abuse and prevent relapse. New vaccines are being developed as therapies for drug or nicotine cessation and relapse prevention. New technologies, such as the production of antibodies in plants, are emerging as cost-effective and efficient ways for the large scale manufacture of immunotherapy agents, represent another facet of this area for development.

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Division of Clinical Neuroscience, Development and Behavioral Treatment (DCNDBT)

A. ***Behavioral Therapy Development Research.*** The Behavioral and Integrative Treatment Branch is particularly interested in research on the development of new or refinement of existing psychotherapies, behavioral therapies, skills training techniques or drug counseling strategies for the treatment of drug abusers/addicts. Incorporation of HIV risk reduction strategies is seen as an integral component in routine counseling or other behavioral interventions for drug abusers. Key products of this research would include the development of: 1) therapy manuals, to define exactly what the therapy is and how to administer it optimally; 2) competence and adherence scales, to evaluate the extent to which therapists and counselors are actually providing the therapy intended; 3) process measures, to measure various aspects of the therapeutic interaction; and 4) measures of the integrity and fidelity of the therapy. The use of technology in developing, administering, and disseminating these products is encouraged, including internet-based programs, CD-ROM technology, audio delivery devices, photo therapeutic instruments, hand-held computers, interactive computer programs, telemedicine, etc. The following topics are of particular interest:

1. *Translation from Basic Behavioral or Cognitive Science.* Development and testing of behavioral therapies or components of such therapies that are based on developments and findings from the basic behavioral or cognitive sciences.

2. *Translation of Cognitive and Affective Neuroscience Findings Towards Development of Behavioral Treatments.* Recent studies using neuroimaging and neuropsychological evaluations provide ample evidence that chronic drug use is associated with neuroanatomical changes that alter cognitive function and the ability to regulate affective states. Further, these changes vary over time and may depend on the current state of the individual (e.g., acute administration of one or more drugs; during initial vs protracted abstinence). Such comorbid conditions make it difficult for many chronic drug users to engage in and participate meaningfully in efficacious behavioral drug treatments. However, knowledge from neuroimaging and neuropsychological studies has not yet been utilized to benefit the patient. In addition, knowledge about fundamental cognitive and affective functioning even in the intact brain, typically has not led to tools that can be used for treating substance abuse. Thus, research that integrates basic research findings on cognition (e.g., decision-making, problem-solving, learning, memory, attention, motivation) and affect (e.g., anxiety, anger, depression) in the following areas are encouraged: Development of interventions to (a) reduce

the negative impact of cognitive dysfunction and affective dysregulation on drug use outcome; (b) prevent relapse; (c) reduce the severity and course of the dysfunctions; (d) improve specific areas of cognitive and affective functioning; and (e) improve daily functioning in addition to reducing clinical symptoms. Other goals of this initiative are to: develop reliable and valid methods for assessing basic cognitive and affective processes as part of clinical diagnosis; evaluate cognitive and affective functioning as indicators of risk for exacerbated drug use during treatment or for developing other disorders; determine if and how current efficacious treatments rehabilitate altered cognitive and affective functioning; modify and test current efficacious treatments tailored to the needs of cognitively impaired individuals.

3. *Treatment of Sleep Disorders for Individuals in Drug Abuse Treatment.* Recent research on sleep has shed new light on its importance to psychological and physical health. Sleep deprivation has been linked with impaired cognitive performance, negative mood, and even decreased immune function. Drug abusers often cite insomnia as reason for relapse, and may use drugs to modulate their sleep/waking cycles. However, the treatment of sleep disorders has not been a primary focus of drug abuse treatment research. The development and testing of sleep hygiene interventions for use in conjunction with drug abuse, as a means of improving treatment for drug abuse is needed. Developmentally appropriate treatment of sleep disorders could impact on the development of more effective treatment interventions.

4. *Modifying Efficacious Behavioral Treatments to be Community Friendly*. Several behavioral interventions have been found to be efficacious for the treatment of drug addiction. However, there are barriers to implementation of behavioral therapies in community-based settings. Community settings that treat drug addicted individuals are reluctant or unwilling to adopt these interventions for a variety of reasons. Reasons that scientifically-based behavioral treatments are not accepted by community providers could include the excessive cost of implementation, the length of time for administration of treatment, inadequate training available for therapists and counselors, treatments not shown to be generalizable for different patient populations or for polydrug abusing populations, etc. Research aimed at modifying efficacious behavioral treatments to make them more acceptable to community settings is needed. Settings might include, drug abuse treatment facilities, primary care, managed care, and the criminal justice system. Examples of possible studies are those that are designed to reduce the cost of implementation of treatments, reduce the time of administration of treatments, aid in training of therapists, counselors and nurses, adapt individual therapies for group situations, etc.

5. *Treatment for Emerging or Specific Populations.* Therapies designed to intervene with understudied populations including users of drugs such as methamphetamine, MDMA and other club drugs, marijuana, and inhalants, as well as personality disordered drug abusers.

6. *Treatment to Prevent Escalation from Abuse to Dependence.* Therapies for drug abusers who are not yet dependent on drugs to reduce risk of escalation to dependence and therapies for drug abusers who have not considered or claim little interest in seeking treatment for their drug problems. For these populations treatments are needed which interest and engage the potential client and intervene with them. Treatments for participants in their natural environment, such as treatments delivered over the Internet or in neighborhood settings such as churches and recreation centers are desired.

7. *Improving Adherence to Medications and Treatment for Drug Abusers with HIV/AIDS.* The introduction of highly active antiretroviral therapy (HAART) has significantly changed HIV/AIDS clinical care. Drug abusers account for a substantial proportion of AIDS cases in the United States, yet have received disproportionately less benefit from highly active antiretroviral therapy than have non drug abusers. Recent studies have shown that HAART is underutilized among drug

abusers, and that individuals who continue to abuse drugs may be less likely to achieve the level of adherence necessary to maintain viral suppression than non-drug abusers. There is a need for research related to the development and evaluation of new and improved behavioral treatments (alone, and in combination with pharmacological treatments for drug addiction), in order to facilitate better adherence to antiviral regimens among drug abusers with HIV infection and also among HIV positive drug abusers who have comorbid mental and/or psychiatric disorders. In the development of behavioral treatment approaches to improve adherence, increased attention to the unique needs of drug abusing women, men who have sex with men, adolescents, and racial/ethnic minority populations is needed. The development and evaluation of innovative medication adherence strategies for HIV positive drug abusers should address issues related to cognitive impairment, emotion regulation, impulsivity, decision-making, motivation, and social and cultural influences. To enhance the utilization of efficacious approaches to improving medication adherence in drug abusers with HIV infection, there is also a need to develop and evaluate treatments administered or assisted by technological devices such as computers, the internet, expert system models, telephone pagers, or hand-held computers.

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8. *Behavioral Strategies for Increasing Compliance in Taking Treatment Medication*. Research to develop and to evaluate strategies to induce recovering addicts to take medication for a prolonged time, especially antagonists such as Naltrexone; to induce HIV infected drug users to comply with medical treatments (HAART) in drug abuse treatment settings; or to adapt existing behavioral strategies to increase patient compliance and cooperation in long-term treatment for drug abuse or for diseases associated with drug abuse such as tuberculosis or hepatitis. An important consideration should be cost and practicality of use in actual clinical practice or in an aftercare program. The product of such research might be a manual, which describes the behavioral strategy, and its implementation by treatment staff or scientific data regarding evaluation.

9. *Integration of Behavioral Therapies and Pharmacotherapies*. Development of integrated behavioral therapies and pharmacotherapies may enhance the efficacy of both types of therapeutic interventions. For instance, the maintenance and detoxification of heroin addicts could perhaps be optimized by the integration of distinctive behavioral therapies devised specifically for opioid agonists, antagonists or partial agonists determined by the heterogeneity of the subgroup of addicts and the pharmacological differences of the medications. Integration of medications and behavioral therapies could possibly enhance compliance with medication regimens, *increase* retention allowing pharmacological effects to occur and prevent relapse to drug abuse and addiction.

10. *Treatment Modules for Specific Problems or Populations.* Discrete therapy components that address specific problems common among drug addicted individuals and that can be implemented in conjunction with other therapeutic services. For example, an investigator may wish to develop a four session, highly focused, job seeking skills module that can be easily implemented by a wide range of practitioners to effectively increase appropriate job seeking behavior. Other examples include, but are not limited to, modules to engage ambivalent drug dependent individuals in treatment, modules to increase assertiveness in female drug addicts who feel pressured by others to use drugs, or to incorporate effective HIV risk reduction techniques.

11. *Behavioral Treatment Research for Drug Abuse and Addiction in Primary Care*. Recent research has shown that physicians and other clinicians often fail to recognize drug abuse or addiction among their primary care patients. In addition, a significant number of these clinicians reported that they did not know how to intervene with their patients if drug abuse

or addiction was suspected. Drug abuse related illnesses and morbidity often occur in adults and may have begun in adolescence. However, very little research has been done to develop or test behavioral treatment approaches or combined pharmacological and behavioral treatments for drug abuse and addiction in primary care settings. The objectives of this initiative are to encourage research on the development and testing of innovative brief behavioral treatment approaches, alone or in combination with pharmacological treatments that may be used in various primary care patient populations and primary care settings. Other goals of this research initiative are to encourage additional research on the development and evaluation of culturally sensitive screening and assessment instruments for use in primary care; and to encourage research on the transportability of efficacious behavioral treatments to primary care settings, as well as research on science-based training approaches for changing primary care clinicians' behaviors regarding their recognition and intervention with drug abusing or addicted patients. While motivational enhancement approaches for some drug abusing populations have been found to be effective, this behavioral approach has not been widely used in primary care.

12. *Using Telemedicine to Disseminate Drug Addiction Research Findings to Primary Health Care Providers*. Telemedicine programs are being used in urban medical centers to rapidly disseminate science-based information on new medical treatments. In addition, approximately one-third of the rural hospitals are now using telemedicine to improve patient care. Health care professionals need science-based information on drug abuse prevention and treatment. Research to develop and evaluate telemedicine programs to transport science-based information on drug addiction to the primary health care community is encouraged.

13. *Developing, Evaluating, and Transporting Culturally Sensitive Behavioral Therapies for Racial and Ethnic Minorities*. Minority populations are disproportionately affected by the consequences of drug abuse. Research to develop and evaluate behavioral treatments that are culturally sensitive and relevant for diverse racial and ethnic minority populations is encouraged. This may include studies of behavioral treatments, alone or in combination with pharmacological treatment, or studies of behavioral strategies for increasing adherence to taking medications. In the development and evaluation of the behavioral treatment, attention needs to be directed at examining medical, social, and cultural factors that may influence adherence to the behavioral treatment approach and treatment outcome. Also, little is known about the transportability of efficacious behavioral treatments for minority populations. Research is needed on how to transport science-based treatments to various racial/ethnic populations.

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14. *Incorporating Smoking Cessation in Drug Abuse Treatment*. Research is encouraged to develop and test behavioral and combined behavioral and pharmacological treatments for nicotine-addicted individuals who also are addicted to other substances, such as heroin, cocaine, methamphetamines and alcohol. Prevalence of cigarette smoking is extremely high among drug dependent individuals attending drug treatment. Many treatment providers are reluctant to address smoking cessation with clients either because they believe that substance abusers are not interested in quitting or because they fear smoking treatment will have a negative impact on drug abuse treatment outcome. However, studies have shown that many drug abuse clients are interested in quitting smoking and that the concurrent treatment of tobacco dependence and other drug dependencies does not threaten abstinence and might even assist in maintaining it. Research is needed to develop and test smoking cessation treatments that can be incorporated into treatments for illicit drugs of abuse.

15. *Developing Treatments for Smokers with Comorbid Disorders*. Research is encouraged that focuses on the development, refinement, and testing of behavioral treatments for smokers with psychiatric comorbidity, such as depression, schizophrenia, or anxiety disorders. Smoking prevalence is very high in individuals with psychiatric disorders. These populations generally respond poorly to traditional smoking cessation treatments. Research is needed to develop and test innovative behavioral and combined behavioral and pharmacological treatments that address the unique needs of these individuals.

16. *Developing Behavioral Treatments for Cognitively Impaired Drug Abusers.* While there are currently many efficacious interventions available for drug addicted individuals in treatment, more can potentially be done to enhance treatments by addressing cognitive impairments that may accompany chronic drug use and HIV infection. Many commonly utilized drug addiction and HIV-risk reduction interventions assume certain basic cognitive capacities and abilities that may be absent, or impaired, in chronic drug abusers who may also be HIV-positive. For substance abusers to benefit from psychological treatment, they must be capable of attending to and receiving new information, integrating it with existing information stores, and translating this input into more concrete behavioral change. Substance abusers with cognitive limitations, who may not comprehend the interventions, are more likely to drop out of treatment, relapse faster, and have poorer long-term outcomes in comparison to cognitively intact substance abusers. Research is needed to develop, modify, and test "cognitive-friendly" drug dependence treatments that could lead to improved treatment response and outcome.

17. *Tobacco Cessation for Pregnant and Post-Partum Women.* Smoking among pregnant women remains an ongoing public health concern. It is estimated that approximately 20-30% of pregnant women smoke. Maternal smoking during pregnancy as been linked to infant mortality, impaired fetal brain and nervous system development, premature and complicated births, and low birth-weight babies. For women who do quit during pregnancy, relapse rates vary, but are reported as approximately 25% before delivery, 50% within four months postpartum, and 70-90% by one year postpartum. Children of smokers continue to be at risk for respiratory illness, middle ear infections, impaired lung function, and Sudden Infant Death Syndrome. Sustained tobacco cessation during pregnancy and the postpartum period reduces health risks to both mothers and their babies. Research focused on the development of innovative behavioral and combined behavioral and pharmacological interventions for nicotine-addicted pregnant and postpartum women is encouraged. Interventions may be tailored to sub-populations of pregnant smokers, such as teenage girls, heavy smokers, or ethnic minorities. Examples of other potential studies may include the development of smoking cessation interventions that address co-occurring issues, such as depression or weight-gain, interventions that include partners or support persons, Internet-based interventions or interventions that can be delivered by primary care physicians.

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18. *Development of HIV Risk Reduction Interventions*. Research to develop and evaluate behavioral strategies to reduce HIV risk behaviors in HIV-positive and HIV-negative substance abusing treatment populations. Where appropriate, risk reduction interventions should be adapted to patients' age, gender, cultural background and potential cognitive impairments, and should address compliance with medical regimens. The product of such research might be training, supervision, or educational materials, such as manuals or videotapes that describe the intervention and its implementation by treatment staff.

19. *Woman and Gender Differences in the Provision of Behavioral Treatments, and HIV/AIDS Risk Reduction Approaches*. Develop and evaluate specific behavioral

treatment approaches targeting drug-addicted women. This may include behavioral therapies, skills training techniques, counseling strategies, and HIV and other infectious disease behavioral risk reduction strategies. This may also include development and testing of training materials that specifically address women and gender differences in drug addiction treatment to promote effective use of research-based treatment approaches. Training materials may involve treatment manuals, training videos, CD ROM or DVD technologies, Internet or computer based programs to manage aspects of treatment administration, or other innovative educational strategies for health professionals using new technologies.

20. *Interventions to Improve Engagement and Retention in Treatment.* Therapies designed specifically to engage and retain individuals in treatment, especially those at high risk for HIV. An example could be a therapy that is: (1) sensitive to the motivational level of the client; (2) is specifically designed to respond to the needs of the individual, whatever his or her motivational level might be; and (3) actively works to increase an individual's desire to remain in treatment.

21. *Complementary and Alternative Therapies (CAT) for Drug Abuse Treatment*. Research is encouraged on complementary and alternative interventions for drug abuse treatment. CAT interventions could be the sole treatment or could be adjunctive strategies to enhance the therapeutic potency of existing drug abuse treatments. An example of an adjunctive CAT intervention might be where the intervention reduces withdrawal symptoms thus enhancing retention in treatment. Included would be interventions that are commonly used in “real world” treatment settings, but whose therapeutic efficacy has not been scientifically demonstrated. Such interventions include acupuncture, bioelectrical stimulation, exercise, biofeedback, meditation, among others. The product of this research might be a manual or video, which illustrates the intervention and how it is implemented by treatment staff.

22. *Development of New or Improved Addiction Assessment Measures and Procedures*. Research directed at the improvement of a currently available measure or the design of a new psychosocial, social or environmental measure appropriate for use in the clinical assessment of substance abusing populations. Special consideration should be given to a specific screening or diagnostic tool, or to a specific measure of treatment readiness, treatment compliance, service utilization, therapeutic process or drug treatment outcome.

23. *Behavioral Therapies for Pre-Adolescents and Adolescents.* Behavioral therapies for pre-adolescents and adolescents that incorporate HIV risk reduction counseling as an integral component of the treatment. This includes the development of new, or refinement of existing psychotherapies, behavioral therapies, and counseling (group and/or individual). This also includes the development and testing of manuals as well as other creative, interactive approaches for therapy delivery that may consider different settings for delivery, such as primary care, school-based health programs, juvenile justice settings, etc. Also the behavioral treatments should be culturally and gender sensitive.

24. *Behavioral Therapies for Couples and Families*. This includes the development of new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious treatments to community settings. Treatments that target domestic violence or other forms of interpersonal abuse along with substance abuse are encouraged.

25. *Behavioral Therapies for Groups*. This includes the development of new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious treatments to community settings. Examples of relevant projects are: traditional group therapies, such as 12-step and therapeutic community approaches, and newer group therapies such as

cognitive-behavioral and acceptance-oriented approaches; groups for various populations, such as adolescents, adults, couple and family groups, gender-specific groups, and groups tailored for racial or ethnic minority populations. Of particular interest are projects that address the recent findings suggesting possible contraindications of group treatments for some populations (e.g., delinquent adolescents), or in some formats (e.g., less-structured, emotion-focused group treatments).

26. *Behavioral Therapies Drawing from Stress Research or Stress-Management Interventions*. Projects are encouraged that apply concepts from stress research (such as appraisal, coping, and social support) to drug abuse in innovative ways, or that test the extent to which stress-management interventions can be applied to the treatment of drug abuse and interventions to reduce risk of HIV and other infectious diseases. Examples of stress-management techniques that may have novel application to drug abuse and HIV risk include techniques that teach problem-solving and affect-management, restore one's sense of purpose and meaning, prevent burnout in the face of chronic stressors, increase self-efficacy for managing stress, inoculate against stressors, train relaxation and meditation, intervene during crises, enlist social support and system support, and others.

27. *Marijuana Treatment.* Marijuana is the most commonly used illicit substance in the U.S. However, relative to other drugs of abuse, little research has focused on the treatment of marijuana dependence. Trends in the literature suggest that the types of treatments effective with other substances of abuse are likely to be effective with marijuana dependence. Initial studies also suggest that many patients do not show a positive treatment response, indicating that marijuana dependence is not easily treated. This solicitation requests research aimed at developing and testing effective interventions for marijuana dependent individuals.

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28. *Transporting Behavioral Treatments to Community Practitioners*. There is a need for effective methods of transferring behavioral therapies found to be effective in clinical trials to clinical practice. Cognitive-behavioral therapy, operant behavioral therapy, group therapy, and family therapy are among the therapies that have been shown to be efficacious in a highly controlled setting and may be helpful treatment approaches in community treatment programs as well. However, community practitioners may have been trained using other approaches and may not have been exposed to these scientifically based approaches. This is a call for proposals that examine mechanisms to transfer effective research-based drug abuse treatment information and skills-based techniques to practitioners in the community. This may involve the development and testing of innovative training materials and procedures to use in the training of community practitioners to skillfully administer these treatments, including the development of highly innovative technology transfer and communication approaches. Research testing the transportability of empirically supported therapies to the community is an important component of the Behavioral Therapies Development Program.

    There is also a need for the development of educational methods to train non-drug abuse health care workers in relating to drug abusers; eliciting medical histories regarding past or present drug abuse; recognition of the signs and symptoms of drug abuse; identification of those at high-risk for HIV and other drug abuse related medical problems such as tuberculosis or hepatitis. Development and validation of a drug abuse screening instrument which can be administered by primary health care providers, and training in administering such an instrument is also needed.

29. *Innovative Technologies for Drug Abuse Treatment, HIV Risk Reduction, and Training Clinicians*. Relevant research would be directed at the development and evaluation of innovative technologies to treat substance abuse, enhance adherence to medications, and/or reduce risk for HIV infection or transmission. Approaches

should be capable of being readily incorporated at reasonable cost into various treatment settings. Areas of interest include Internet-based treatment or training programs, CD-ROM technology, audio delivery devices, photo therapeutic instruments, and hand-held computers. Also of interest are creative approaches for disseminating science-based behavioral treatments and for training therapists to use scientifically based treatments for drug abuse and addiction. Such approaches might include Internet-based education, interactive computer programs, telemedicine, etc. Finally, approaches which apply therapies with evidence of efficacy through new media such as web-based platforms, over email, or through chat rooms and bullet boards are also desirable.

30. *Virtual Reality Applications for Drug Abuse Treatment Provider Training*. Recently virtual reality simulations have been used to train medical personnel in demanding medical procedures such as microsurgery techniques. Virtual training allows trainees to gain familiarity with both the environment in which services are delivered as well as the intervention techniques without the danger of mistakes impacting live patients. Virtual reality interfaces can assess skill acquisition and provide detailed feedback during procedures to help trainees correct mistakes or avoid making them altogether. In the drug abuse field, training and dissemination efforts have been hampered by a dearth of knowledge about ways to conduct dissemination. Although trainees often practice on actual clients, this approach has drawbacks including its reliance on the client or participant's schedule and willingness to participate in training sessions and potential danger to the client or if the intervention is delivered incorrectly. Libraries of virtual reality simulations of drug users in treatment or "virtual patients" are needed to provide experiential training for treatment providers without relying on existing patients. This will help facilitate the rapid and effective dissemination of proven treatment strategies.

    Development and improvement of treatments using Virtual Reality and other new technologies is also needed. New technology may help to make existing treatments more effective, or may make novel treatments possible. Behavioral treatment research to develop, modify, adapt, and test treatments for drug abuse and for comorbid psychiatric conditions (such as anxiety disorders) using new technologies is of interest.

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B. ***Clinical Neuroscience Research.*** The Clinical Neuroscience Branch (CNB) supports research on the biological etiology (determining the biological basis for vulnerability to drug abuse and progression to addiction, including studies on individual differences and genetics) and clinical neurobiology of addiction (exploring alterations of the structure and/or function of the human central nervous system following acute or chronic exposure of drugs of abuse), and the neurobiology of development (neurobiological effects of drugs of abuse and addiction during various stages of development and maturation, effects of drug exposure on neurobiological processes, development of methodologies and refinement of techniques used in pediatric neuroimaging). The Branch also supports investigations on the cognitive neuroscience of drug abuse and addiction, the neurobiology of treatment, neuroAIDS, and human pain and analgesia. Areas that may be of interest to small businesses include, but are not limited to:

1. *Development of Novel Approaches in Human Neuroscience.* Development of innovative, noninvasive research methods or novel approaches are needed to identify various neurobiological markers of brain alterations in humans induced by acute or chronic exposure to drugs of abuse. This may include the identification of neurobiological (including genetic) markers that might be associated with risk for, or resilience to drug abuse and addiction. Of particular interest are noninvasive methods (e.g., brain imaging) that could be used to determine the effects of drug abuse/ addiction treatments on neurobiological systems in an attempt to understand the neurobiological processes underlying therapeutic efficacy.

In recent years, there has been an increase in studies employing functional magnetic resonance imaging (fMRI) to understand brain processes and functional neuronal systems. In particular, these neuroimaging techniques are being used to probe how drugs of abuse alter brain functioning. Consequently, there is a need for the development of stimulus generation hardware to be used within an fMRI magnet that can display stimuli important in drug studies. As the studies of brain function become more sophisticated, task-related assessments of brain activation are increasingly important. Shielded goggles or other types of stimulus-generating hardware and software are necessary for presentation, for example, of neurocognitive tasks, drug-related images for the induction of craving, or other "virtual reality" types of dynamic stimuli important in studies of drug abuse and addiction. Responses to this type of stimulation then could be correlated with brain measures using neuroimaging techniques. These types of studies will provide new insights into drug-brain-behavior interactions.

Development of the human central nervous system and how drugs of abuse perturb this process is of great interest. Little is currently known about the effects of exposure to drugs of abuse, either prenatally or during childhood or adolescence, on the development of the human nervous system. Further, the application of newly emerging technologies (such as neuroimaging) to these populations presents unique challenges due to the fact that the central nervous system, and its capabilities, are changing rapidly. The development of novel techniques, or the refinement of existing methods, to provide direct noninvasive measures of brain structure and/or function that are adapted specifically for use in pediatric and adolescent populations is strongly encouraged. Also, neurocognitive and other neurobehavioral tasks for use in these populations, especially where they can be designed to probe underlying neurobiological processes, need to be developed (for developmental issues, contact Laurence Stanford, Ph.D.).

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2. *Virtual Reality for the Neurobiological Study of Drug-Brain-Behavior Interactions and Drug Abuse Treatment.* Virtual Reality (VR) is an emerging technology useful in a variety of research-related, therapeutic and instructional settings. By immersing a person's senses in a synthetic world or Virtual Environment (VE) that characterizes VR, a highly flexible and programmable set of stimuli can be used to enhance the standard approaches used in assessment of neurobiological and neurobehavioral processes.

   Collection of real-time data and bulk data recording can provide a correlation of a stimulus reference signal with simultaneously collected fMRI scanner and physiological data over time. Unlike most computer access systems that accept only one or two modes of precise and/or discrete input at a time, VR systems have the potential to monitor movement or action from any, or many, neurobiological functions at once. In addition, the multimodal feedback inherent in VR provides a way to vary nonvisual stimulus components (e.g., resistance, temperature, pitch) in a way that is impossible to achieve via standard computer systems. Finally, VR systems provide a bypass for keyboard entry or direct manipulation environments (e.g., pointing instruments like the mouse), by allowing the manipulation of multi-sensory representations of entire environments by natural actions and gestures.

   VE can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction. For example, VR allows for the presentation of a variety of complex, multi-sensory stimuli for neurocognitive tasks or, alternatively, the dynamic stimuli important for producing drug-related images for the induction of craving. VR can also be tested as an

alternative to traditional behavioral therapies in the treatment of drug abuse. Responses obtained as a result of the above can then be correlated with brain measures using state-of-the-art neuroimaging techniques. We, therefore, invite studies employing VR, especially to probe brain processes in drug abuse/addiction combined with neuroimaging methods or to be developed or applied as a potential treatment for substance abuse.

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3. *Development of Interactive Computer Applications for Neuropsychological/ Neurocognitive Assessment to Determine Functional Brain Deficits in Acute and Chronic Drug Abusers.* In addition, a neurobehavioral test battery to assess other neurobehavioral/neurocognitive deficits resulting from drug abuse/addiction is encouraged. Of particular interest is the development of such assessments for use in children and adolescents exposed to drugs of abuse to better define and understand the effects of early exposure on brain function and development (for developmental issues, contact Laurence Stanford, Ph.D.).

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4. *Development of Ligands for Brain Imaging.* Development of novel radioligands for PET and SPECT imaging in human brain for molecular targets (e.g., receptors, intracellular messengers, disease-related proteins) is of broad interest to the neuroscience and drug abuse research community. The primary application of these radiotracers will be in basic neuroimaging research. Ultimately, these radiotracers may also be used as potential biological markers and surrogate endpoints for translational and clinical research, drug discovery and development, and clinical trials. The scope of the projects may encompass pilot or clinical feasibility evaluation in pre-clinical studies, model development, or clinical studies. Alternatively, the focus may be on research and development of new technologies for radiotracer development.

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5. *Novel Approaches in the Clinical Neurobiology of Drug Addiction.* Many scientists involved in behavioral and neurobiological research are faced with growing difficulties in identifying approaches, devices (e.g., research tools) and/or strategies to broaden the within-discipline knowledge base for understanding, preventing and treating drug abuse. NIDA has a strong interest in facilitating the identification and use of cross-disciplinary research tools and materials that are being used and have proven efficacious in research unrelated to drug abuse (e.g., virtual reality, transcranial magnetic stimulation, deep brain stimulation). NIDA also has a strong interest in promoting the commercial adaptation and widespread availability of discoveries (“tools”) made in the course of interdisciplinary research to better serve its mission.

   The term research “tool" is being used in its broadest sense to embrace the full range of resources that scientists use in the laboratory and clinicians use as therapeutics; therefore, one investigator’s tool may be another's end product. The value of research tools is difficult to assess and varies greatly from one tool to the next and from one situation to the next. Providers and users are likely to differ in their assessments of the value of research tools. Many research and clinical tools are costly to develop and have significant competitive value to the firms that own them.

   Advances in biomedical science continuously yield new research findings that play a critical role in the furtherance of knowledge and innovation in both the public and private sectors. For the purpose

of this solicitation, the term research tool may include methods, laboratory equipment and machines, databases and computer hardware and software. From a clinical perspective, interactive games and emerging game technologies are being used successfully in a variety of health education situations; therefore, applications proposing introducing these "tools" as adjuncts in the prevention and treatment of drug abuse will be accepted. NIDA has solicited and continues to solicit proposals using virtual reality to increase our understanding of the neurobiology of addiction, (e.g., drug cues, craving), comorbidity (e.g., post-traumatic stress disorders) and pain (e.g., distraction). Additional novel approaches, devices and strategies are now being sought to further our understanding of the cognitive neuroscience of drug abuse and addiction, neuroplasticity and repair, the neurobiology of treatment (including training tools, assessment and neurolobiologic correlates of treatment outcome) and neuroAIDS.

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6. *Development of Serious Games for Neuro-Rehabilitation of Drug-Induced Cognitive Deficiencies.* Health-related gaming is an emerging industry useful in a variety of research-related, therapeutic and instructional settings. Serious games can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction.

   By involving a person in an interactive computerized situation, designed to be both entertaining yet directive (i.e., in the sense of covertly shaping desired behaviors via highly flexible and programmable sets of scenarios), altered behaviors can be introduced by pre-programming consequences to counteract and potentially reset undesirable neurobiological and neurobehavioral deficits associated with chronic drug abuse.

   It is hypothesized that changes in behavioral contingencies as a consequence of varying time and/or rate of the stimulus-response-reinforcer sequence (e.g., designing a game that involves differential rates for low responding (DRL) schedule) may alter brain activity (pattern changes noted using state-of-the-art neuroimaging techniques) and, thus, correlate with the improvement of neurocognitive deficits

   Neurocognitive deficits are generally drug-specific. For example, chronic methamphetamine abusers loose their decision-making ability, and suffer attentional bias in a visual discrimination task. Cocaine abusers lack cognitive flexibility, the ability to use feedback to monitor/change behavior, have slower reaction times on match-to-sample and increased errors (both omission and commission) along with attention/concentration deficits. Chronic use of opiates produces an increase in auditory, visual, and associative reaction times, impaired vigilance, attention, information processing, short-term visual memory, delayed visual memory, short-term verbal memory, long-term verbal memory and problem solving. Although in controversy, marijuana may decrease one's ability to focus, sustain, and shift attention as well as decrease memory and motivation.

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C. ***Human Development Research.*** The Behavioral and Brain Development Branch (BBDB) supports a broad research, research training and career development programs directed toward: (1) an increased understanding of how developmental processes and developmental outcomes are affected by drug exposure and related factors; (2) an increased understanding of developmental processes that are relevant to: (a) drug use, abuse, addiction, treatment and relapse, and (b) risk behaviors related to drug abuse and other health conditions that often accompany drug use (*e.g.,* HIV infection, STDs); (3) the use of translational approaches to increase understanding of these developmental processes; and (4) an increase in effective interventions aimed at preventing or ameliorating negative developmental outcomes

resulting from exposure to drugs and related factors.

1. *Develop Improved Technology for Assessment of Prenatal Drug Exposure and Passive Postnatal Drug Exposure.*

   a. Develop and refine methods for the detection and quantification of infant exposure to drugs of abuse during pregnancy, including cocaine, marijuana, opiates, and methamphetamines.

   b. Develop and refine methods for the detection and quantification of passive exposure to illicit drugs during infancy and childhood.

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2. *Develop Interactive Database Systems on Human Subjects Issues for Use by Drug Abuse Researchers Studying School-Age Children and Adolescents Drug Use.* Develop systems to assist investigators in obtaining technical and legal information relevant to involvement of children and adolescents in research on drug abuse. Examples of pertinent situations include tracking long-term health and development of children exposed to drugs during pregnancy, and investigating vulnerability and possible pathways to drug abuse among school-age children and adolescents. These database systems should address issues such as assent and consent, should provide information on variation in laws and guidelines across jurisdictions, should include the capacity for interactive communication on numerous situations potentially facing investigators, and should serve as sources of referral for additional assistance.

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3. *Develop Improved Methods of Neuroimaging to Assess Structural and Functional Status of the Brains of Children and Adolescents Exposed to Drugs.* Document the feasibility and accuracy of appropriate and acceptable methods for assessing brain structure and function of children and adolescents, with special attention to any or all of the following groups: those exposed to drugs during pregnancy, those passively exposed during infancy and childhood, and those actively using illicit substances. Documentation should include attention to such matters as technological difficulties and risks, and standardization issues relevant to testing conditions and image analysis.

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4. *Develop and Refine Methodologies for Drug Use Measurement Among Adolescents.* Research to develop and refine methodologies for drug use detection and quantification, with special application to the adolescent with HIV infection or at high-risk for HIV infection. This research should address issues of acceptability, reliability, and validity of one or more methods (e.g., interviews, computerized questionnaires, and biological indicators such as saliva or sweat).

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Division of Basic Neuroscience and Behavioral Research (DBNBR)

DBNBR's basic neuroscience and behavioral research focuses on understanding the mechanisms, characteristics, and processes of drug abuse. Basic behavioral, cognitive, neurobiological, cellular, molecular, chemical, and genetics research aims at characterizing and understanding drug seeking, compulsive behavior, and addictive processes. These research areas necessarily include studies of normal processes.

Using both animal and human studies, basic behavioral research focuses on behavioral and cognitive processes that may or do lead to drug initiation, and the behavioral and cognitive consequences of drug abuse. Neurobiology research focuses on the neural mechanisms and substrates underlying behavioral and cognitive processes and vulnerability factors associated with drug abuse, addiction, sensitization, tolerance, and relapse. DBNBR supports basic chemistry and pharmacological studies focusing on structure/activity relationships, definition, and

characterization of systems involved in drug actions, chemical synthesis of new ligands, pharmacokinetics, analytical methods, understanding basic mechanisms of drug action and drug testing.

Computational and theoretical modeling of biological systems and behavioral processes, biomedical computing and/or information science and technology development is supported by DBNBR.

1. *Nanoscience-based Design of Therapies for Substance Abuse Treatment.* Nanoscience and nanotechnology, by manipulating matter at the atomic or molecular levels, are emerging research areas that have the potential to fundamentally transform the study of biological systems and lead to the development of new methods for detection, prevention, and treatment of substance abuse and related disease states. NIDA invites nanotechnology-based applications in the following areas:

    a. Methods to enhance the efficacy of FDA-approved compounds by reducing their size to the nanoscale range to alter absorption, distribution, metabolism, or excretion.

    b. Development of new compounds, through manipulation of matter at the atomic or molecular levels that could more readily pass the blood-brain-barrier or cell membranes.

    c. Development of nanoscale particles for controlled targeted delivery of therapeutics, genes, or antibodies.

    d. Methods to enhance existing imaging technologies using magnetic properties at the nanoscale.

    e. Application of nanostructures (e.g. noble metal nanoparticles, quantum dots, and nanolithographic structures that show promise for diagnostic development) for identification and analysis of genes, proteins, and other biological molecules implicated in the actions of drugs of abuse.

    Proposals are invited from any of the above areas. Phase I should demonstrate convincingly the viability of the proposed innovation, whereas Phase II should carry out the development, characterization, testing, and screening of the innovation.

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2. *Virtual Reality for Treatment of Pain.* Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) exposure can reduce reported pain during wound care. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of pain. Development of treatments for both acute and chronic pain is sought. These treatments can be based in clinical settings or the patients' homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.

3. *Virtual Reality for the Treatment of Drug Abuse.* Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to ignore drugs cravings, withdrawal symptoms or environmental cues that promote drug abuse. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of drug abuse. These treatments can be based in clinical settings or the patients' homes. These treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies to address abuse of all types of drugs (e.g., cocaine, marijuana, nicotine, alcohol, inhalants) are sought. Phase I testing should establish the feasibility of the use of this technology for the particular drug problem addressed (e.g., cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should

involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

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4. *Development of a Virtual Reality Environment for Teaching about the Impact of Drug Abuse on the Brain.* Virtual reality (VR) is emerging as a technology with a multitude of uses within the medical sciences. In terms of the science of drug abuse, it is being developed as a treatment tool. The current solicitation seeks the development of a virtual reality environment that can be used in educational settings to teach about how drugs of abuse (both illicit and licit) affect the brain and behavior.

   The cost of portable hardware needed to present a VR environment is relatively inexpensive. If education programs like the one sought in this solicitation were available, it is likely that VR would be used as a teaching tool in many settings, including classrooms and museums.

   The particular program sought here is to present an interactive three-dimensional virtual brain that shows normal brain functions and, in contrast, brain function after exposure to drugs of abuse. This technology could illustrate the neurotoxic and long-term effects of drug abuse on the brain. This VR may include other features that are not described above, provided that it will be useful in educating individuals about the medical, behavioral and social effects of drug abuse.

   The phase I proposal should develop a beta version of the program. Further, the phase I application should include a preliminary demonstration of “usability,” where it is shown that the types of people being educated with this program (e.g. teachers) can effectively operate this system without extensive training. Further, it should be demonstrated that the hardware is easily worn by subjects, and that the subjects can rapidly understand how to effectively interact in the VR environment.

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5. *Chemical Libraries for Drug Development.* The development and biological screening of lead compounds and their combinatorial libraries for use in the area of drug abuse treatment research are encouraged, such as generation of new ligands having opiate receptor selectivity, or ligands with NMDA or serotonergic agonist/antagonist activity and/or related ligands. These would be designed as lead compounds either for drug design or as tools to elucidate mechanisms of action of drug abuse.

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6. *Genetic Studies.* The National Institute on Drug Abuse is interested in SBIR proposals that would facilitate the identification of genetic loci that confer vulnerability to substance abuse and addiction. Areas of interest include but are not limited to:

   a. Collection and genotyping of human pedigrees and sib-pairs for vulnerability or resistance to drug abuse.

   b. Isolation and identification of mutant strains in genetic model systems such as Zebra fish, Drosophila, C. elegans, mice, and rats that are more vulnerable or resistant to drugs of abuse.

   c. Design, development, and marketing of behavioral apparatuses to conduct rapid behavioral throughput screens for identifying genetic vulnerability to addiction in genetic model systems.

   d. Development of transgenic models for drug abuse using bacterial artificial or yeast artificial chromosomes.

   e. Development of software and databases for candidate genes for drug abuse.

   f. Identification and mapping of functional polymorphisms of candidate genes for drug abuse.

   g. Placement of candidate genes for drug abuse on biochips.

   h. Marker-assisted breeding of congenic mouse and rat strains for mapping quantitative trait loci associated with addiction and drug abuse.

i. Vectors for gene transfer into neurons.

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7. *Drug Testing Development.* Development of new, more refined or more practical drug testing methodologies. Studies may focus, but are not limited to the following topics: drug testing methods; drug extraction procedures; methods to control for possible environmental contamination factors; and reference materials. Methodologies with special application to the workplace, the emergency room, the transportation environment, or other specific settings are welcome. Methodologies with an emphasis upon circumstances for testing such as post-accident testing or readiness for work testing are also encouraged.

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8. *Effects of Drugs at the Cellular Level.* Development of new imaging techniques, reagents and related hardware and software for dynamic investigations of the effects of drugs of abuse on cellular activities and communications. For example, these techniques might include, but are not limited to, development and utilization of reagents for magnetic resonance microscopy and other MRI methods; development of methodologies applying functional MRI to drug abuse studies; the use of dyes, intrinsic signals, and other optical indicators for studying signal transduction mechanisms, the regulatory control of protein entities (such as phosphorylation), and neuronal excitatory and inhibitory pathways. Areas of interest may include, but are not limited to:

   a. Studies using molecular biological techniques to scale-up protein production for investigations aimed at enhancing understanding of the structure, function and regulation of molecular entities involved in the cellular mechanisms through which abused drugs act.

   b. Validated in vitro test systems can reduce the use of animals in screening new compounds that may be of potential benefit in treating drug abuse. Test systems are needed to evaluate activity at receptors or other sites of action, explore mechanism(s) of action, and assess potential toxicity.

   c. With the recent success in molecular cloning of various drug abuse relevant receptors, enzymes, and other proteins, researchers will elucidate the molecular mechanism of action of these drugs. Studies to generate strains of transgenic animals carrying a gene of interest are solicited. Of special interest are knockout and tissue-specific knockout animals. These animals can be used to identify gene function, and to study the pharmacological, physiological, and behavioral role of a single gene.

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9. *Toxicity Studies*

   a. Studies on abused drugs and their metabolites to develop methodologies that may be potentially useful in addressing medical emergencies. Such studies might include investigations involving development of pharmacokinetic models, methodologies, and data.

   b. Concern remains about the potential acute and chronic neurotoxicity of drugs of abuse. Information is needed about the possible neurotoxicity of pharmacotherapeutic agents with potential for treating drug abuse. Improved methods are needed for identifying, assessing, and quantifying the nature and extent of neurotoxicity. Such studies might include the development or application of quantitative chemical, physiological, or behavioral measurements relating to nervous system injury or methods for quantitative analysis of damage.

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10. *Predisposition to Cardiovascular Complications Associated with Abused Substance(s).* Development of experimental animal models to assess a genetic predisposition or increased sensitivity to cardiac and vascular complications associated with drug use. Such studies might include, but are not limited to, investigations involved with biochemical,

physiological and pathological indices of cardiovascular system function.

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11. *Opioid Peptides.* Research and development directed at the medicinal chemistry and molecular pharmacology of opioid peptides, especially in methods development. Areas of interest include but are not limited to:

    a. Development of innovative methodologies for the synthesis of opioid peptides to be made available to researchers. Syntheses proposed should be limited to single analogs.

    b. Methods to identify new ligands for opioid receptors and the design of new opioid peptide analogs with therapeutic potential.

    c. Development of analytical methodologies for the quantitation of synthetic and endogenous opioid peptides, peptide precursors, and processing enzymes. The innovation may be limited to a part of the method, such as development of a special detector or a sample cell. Methods might include antibody development and development of innovative immunoassays.

12. *Ligands for receptors of drugs of abuse.* Applications are solicited using chemical combinatorial library techniques or traditional synthetic methods, to develop ligands having a high degree of efficacy and selectivity, antagonists, partial agonists, inverse agonists, neutral agonists to receptors of drugs of abuse such as for dopamine and serotonin receptors, DA and 5-HT, NE transporters, nicotine receptors, cannabinoid receptors, excitatory amino acid receptors, m-Glu receptors, opioid receptors, GHB receptors and others. These can be useful both as pharmacological tools and lead compounds in medicinal chemistry/drug development.

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13. *Cellular Systems Biology.* The National Institute on Drug Abuse is interested in SBIR proposals that would facilitate global analysis of biological systems relevant to drug abuse. Technologies and resources developed should be applicable and relevant to drug abuse research. Areas of interest include, but are not limited to:

    a. Improved technology for analysis of membrane proteomes for the identification of targets and validation of leads.

    b. Development of technology or new strategies that will improve dynamic range to allow the analysis of a broader spectrum of the proteome of neural cells.

    c. Single cell analysis and the development of model systems for proteomic analysis of neuronal function and drug effects.

    d. Development of real-time proteomics technology for the analysis of processes such as cellular responses to drug exposure.

    e. High throughput, high resolution 3-dimensional in situ proteome profiling such as optical projection tomography, improved methods for high throughput sectioning of neural tissue and the development of tools for identifying and mapping protein expression, localization and movement relevant to addiction and other medical consequences of drug abuse.

    f. High throughput, functional, molecular interaction screening methods for proteins implicated in drug abuse.

    g. Strategies to characterize post-translational modifications related to addiction and drug effects.

    h. Development of proteomic tools for identifying biomarkers to track therapeutic efficacy, to monitor effects of drug interactions, and to advance biological understanding of relationships between drug use and infectious disease, and therapies for HIV, hepatitis C and other diseases.

    i. Technologies to identify parameters of molecular, cellular, or physiological systems important in addiction, and the properties of the system, such as redundancy and robustness.

    j. New approaches for characterizing cell phenotypes and mapping those phenotypes.

    k. Development of other novel technologies using non-mammalian animal model

systems or new approaches for sensing and analyzing cell components and activities (such as quantum dots).

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14. *Research Resources.* The National Institute on Drug Abuse is interested in SBIR proposals that would generate the following resources for drug abuse research:

    a. Resources for the application of genetic engineering to dynamically monitor neuronal function.

    b. C57BL6 Mouse embryonic stem cells and spermatogonial stem cells.

    c. Turnkey technology for proteomics such as the development of protein and peptide chips to study drug effects on neuronal mechanisms.

    d. Antibodies, aptamers, ligands, etc. relevant to drug abuse research.

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15. *Development of Innovative Synthetic Probes, Drug Dosage Forms, and/or Drug Metabolites For Drug Abuse Research.* Proposals are solicited for the synthesis of new chemical compounds, drug metabolites, peptidomimetics, and/or development of drug dosage forms for studying the mechanism of action of drugs of abuse and drug addiction.

    Specifically proposals are encouraged in the following areas:

    a. Synthesis of chemical probes, drug metabolites, peptidomimetics, and/or development of drug dosage forms that are needed by drug abuse research investigators and not commercially available, or difficult to obtain.

    b. Alternate synthetic methods for existing chemical probes that improve the yield and produce these chemicals at lower costs as compared to commercially available substances.

    c. Development of alternate drug dosage forms of existing drugs/drug products for enhancing their efficacy.

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16. *Development of Analytical Techniques.* The development of new analytical methods for measuring drugs of abuse and their metabolites in biological matrices, such as urine, blood, saliva, sweat, hair, breast milk, brain tissue, and meconium is encouraged. The new methods should be efficient, sensitive, convenient, and cost effective. Modifications and improvements in existing analytical techniques are also encouraged particularly those improving sensitivity and selectivity.

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17. *Metabolomics in Drug Abuse Research.* Metabolomics is the study of all the molecules of a cell or organism and their identification and quantification that helps to understand the cellular regulation, metabolic pathways and activity and response under normal and other conditions. This technique thus could be used to develop metabolic profiling of normal or healthy subjects and subjects under the influence of substances of abuse or those undergoing drug rehabilitation. NIDA is seeking proposals to develop metabolomic profiling of subjects under the influence of drugs of abuse to identify and characterize biomarkers for understanding the addictive disorder. Proposals using animal and/or human model studies are welcomed. Phase I proposals should demonstrate the feasibility of metabolic profiling and phase II should focus on the application of this invention in identifying and characterizing responsible biomarkers.

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18. *Computation, modeling and data integration in Drug Abuse Research.*

    a. Development of software or other tools, which enable data integration, and the

development of computational models related to addiction and other medical consequences of substance abuse, e.g. tools that enable the integration of proteomics, genomics, transcriptomics, metabolomics and other data into applications leading to systems understanding of drug effects upon biological systems, or developing innovative approaches for managing knowledge and integrating information from text, data, image, and other sources or files generated in addiction research.

b. Tools that enable multilevel and multiscale modeling of biological and behavioral systems relevant to substance abuse research, such as those relevant to evaluations of expected utility.

c. Development of software tools and interactive technologies (such as applications of grid technologies and networked appliances) which enable the prevention, study, and treatment of substance abuse as well as the evaluation of prevention and treatment strategies.

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19. *Tools and Resources for Epigenetics Research.*

Some of the long-term effects that occur in addiction may be attributed to epigenetic changes. As researchers begin to investigate these changes as a mechanism leading to addiction, several tools and resources would be needed. Phase I should demonstrate feasibility of the approach. Phase II is for production of the resource.

a. Development of a new battery of HDAC isoform-selective inhibitors that cross the blood-brain barrier.

b. Transgenic mice containing knock-in tandem affinity tags (which would allow definition of transcription factor binding sites for any factors of interest).

c. Methods for determining the subcellular localization of microRNAs.

d. Technical innovations to allow genome-wide screening for changes in DNA methylation.

e. Development of antibodies to chromatin regulatory proteins.

f. Creation of tools to allow unambiguous labeling of a specific amino acid on a specific histone in a specific gene region.

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Division of Epidemiology, Services and Prevention Research (DESPR)

A. ***Prevention Research Branch (PRB).*** The Prevention Research Branch (PRB) supports a program of research in drug abuse and drug related HIV prevention to (1) examine the efficacy and effectiveness of new and innovative theory-based prevention approaches for drug abuse, drug-related HIV/AIDS and other associated health risks, (2) determine the cognitive, social, emotional, biological and behavioral processes that account for effectiveness of approaches, (3) clarify factors related to the effective and efficient provision of prevention services, and (4) develop and test methodologies appropriate for studying these complex aspects of prevention science.

Prevention Research. Rigorous scientific prevention research is encouraged to study novel approaches to substance abuse prevention for use at multiple levels of the social environment including: the family, schools, peer groups, community and faith-based organizations, the workplace, health care systems, etc. The purpose of this research is to determine the efficacy and effectiveness of novel program materials, training strategies, and technologies developed to prevent the onset and progression of drug abuse and drug-related HIV/AIDS infection. Materials and technologies may target a single risk-level or may take a comprehensive approach encompassing audiences at the universal, selective, and/or indicated levels. Universal interventions target the general population; selective target subgroups of the population with defined risk factors for substance abuse; indicated interventions target individuals who

have detectable signs or symptoms foreshadowing drug abuse and addiction, but who have not met diagnostic criteria. NIDA encourages the development and testing of innovative prevention intervention technologies that are sensitive and relevant to cultural and gender differences.

1. Laboratory studies of the underlying mechanisms and effects of various prevention approaches such as persuasive communication (e.g., mass media and print media) as they are affected by and affect drug related cognition, emotion, motivation and behaviors.
2. Decomposition of prevention programs to understand components that account for program effectiveness.
3. Research on features of prevention curricula, materials, implementation, approaches, training, technical assistance, and systems integration that contribute to positive outcomes.
4. Training modules and ongoing technical assistance for program implementers of research based substance abuse prevention programming strategies.
5. Prevention intervention dissemination technologies and mechanisms that integrate research with practice; specifically the transfer of drug abuse prevention information to decision-makers, funders, and practitioners.
6. Prevention services research on the organization, financing, management, delivery, and utilization of drug abuse prevention programs.
7. Strategies for the integration of proven prevention approaches into existing service delivery systems.
8. Studies that develop and assess reliability and validity of developmentally appropriate self-report, physiological, and biochemical measures for use in prevention trials in a variety of settings and a variety of audiences.
9. Development of and testing of environmental change strategies for schools, neighborhoods, communities, etc. to use in reducing substance use initiation and/or progression.
10. Development of community needs assessment tools and services.
11. Drug abuse prevention methodological research on promising data collection, data storage, data dissemination, and reporting techniques.

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B. ***Epidemiology Research Branch (ERB).*** The ERB supports a research program on drug abuse epidemiology that includes (1) studies of trends and patterns of drug abuse and related conditions such as HIV/AIDS in the general population and among subpopulations, (2) studies of causal mechanisms leading to onset, escalation, maintenance, and cessation of drug abuse across stages of human development, (3) studies of person–environment interactions, (4) studies of behavioral and social consequences of drug abuse, (5) bio-epidemiologic studies including genetic epidemiology studies, (6) methodological studies to improve the design of epidemiologic studies and to develop innovative statistical approaches, including modeling techniques.

1. *Improvement of Reliability and Validity of Reporting of Sensitive Data*. The reliability and validity of self-report of drug use and related behaviors (e.g., HIV risk behavior) is a matter of great concern. Use of new technologies for real time data collection in ecological settings is of great interest because these technologies enable collection of drug consumption data in context. Studies to improve methodologies based on variations of standard survey protocols or computer-assisted self-interview (CASI) and personal interview (CAPI) are also encouraged.
2. *Instrument Development.* Easy-to-use assessment instruments are needed to enhance epidemiology research. Areas of interest include but are not limited to:
   a. *Community Assessment.* The development of community diagnostic instruments for psychometrically sound assessment of community characteristics is essential to improve our understanding of how community factors affect drug abuse and ensuing behavioral and social consequences.

Standardized assessments of community characteristics are needed to better understand the full impact of drug use and to develop targeted interventions to specific community needs.

b. *Assessment of Psychiatric Comorbidity in Community Settings.* Easy to use, reliable, and valid instruments are needed to assess psychiatric comorbidity in different populations of drug abusers, including adolescents and those in community drug abuse treatment settings.

c. *Assessment Instruments to Measure CNS Function Related to Drug Abuse.* The development of age-appropriate assessment instruments to measure behavioral and cognitive function over the course of development will contribute to our understanding of vulnerability to drug abuse and functional impairment due to drug use.

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C. ***Services Research Branch (SRB).*** The SRB supports a program of research on the effectiveness of drug abuse treatment with a focus on the quality, cost, access to, and cost-effectiveness of care for drug abuse dependence disorders. Primary research foci include: (a) the effectiveness and cost-benefits and cost-effectiveness of drug abuse treatment, (b) factors affecting treatment access, utilization, and health and behavioral outcomes for defined populations, (c) the effects of organization, financing, and management of services on treatment outcomes, (d) drug abuse service delivery systems and models, such as continuity of care, stages of change, or service linkage and integration models, and (e) drug abuse treatment services for HIV seropositive patients and for those at risk of infection.

1. *Drug Abuse Treatment Economic Research*. This initiative will support research to design and develop data systems for financial management and economic analysis of treatment programs and larger systems in new healthcare settings and managed care networks. Managerial decision-making requires the implementation of sophisticated data systems to facilitate routine budgeting processes, allocation of resources, performance measurement, and pricing decisions. The focus is on the needs of managers within the organization and managers outside of the organization. Data system development must be based on standard cost behavior and profit analysis. Data systems must be designed with correct cost concepts (accounting and economic) in order to permit cost and pricing decisions to be developed for new treatment technologies and management of on going systems. In research settings, such an initiative is vital for the assessment of new technologies developed for transfer to practice.

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2. *Personnel Selection Technology Research for Drug Abuse Treatment Clinics*. Research is showing that employee turnover is a substantial problem among substance abuse treatment services providers. Applications supporting innovative research that develops and validates generic staff selection systems which could be adopted and tailored for use by drug abuse treatment clinics are welcome. Like many small businesses, drug abuse treatment clinics have problems attracting and retaining qualified personnel. Also like many small businesses, treatment clinics have limited resources to apply to the recruiting, screening, and hiring of new and replacement personnel. Research has shown that the application of standardized screening and selection methods designed to maximize person-job fit can cost-effectively reduce staff turnover. Systematic methods such as background inventories, protocol-driven interviews, aptitude tests, and credit checks have demonstrated validity for improving person-job fit. Examples of possible projects might include development of easy-to-understand guidance about legal considerations in hiring practices, software that transform job task analysis into selection criteria, interview protocols to standardize applicant screening, tolls to help improve recruitment,

and/or self-paced training for hiring officials or interview panels to improve screening reliability.

3. *Customer Retention Technology*. Premature disengagement from drug abuse treatment participation is a common problem and ranges from approximately 30 to 60% based upon the clinic and modality studied. Past research has very frequently attributed dropping out of treatment to participant characteristics (e.g., motivation, addiction severity, comorbidity) and/or environmental factors (e.g., social pressures, unemployment, homelessness). Seldom has the dropout problem been studied in the context of customer satisfaction. That is, there is little research looking at the causes of dropping out of treatment attributable to organizational factors (e.g., policies, practices, context) that influence participant withdrawal decisions. Needed are tools and systems for assessing and surveying drug abuse treatment program participant perceptions and satisfaction levels, summarizing and report participant assessments, interpreting results, and adjusting policies and practices to improve satisfaction and participant retention in treatment.

4. *Effective Management and Operation of Drug Abuse Treatment Services Delivery*. The bulk of drug abuse treatment is conducted in small clinical settings with therapeutic staffs of less than a dozen people. Small clinics lack resources to help improve efficiency and effectiveness in both business and therapeutic practices. Areas that may be of interest to small businesses include, but are not limited to:

   a. Computer-based leader/manager self assessment tools: On-line and other types of tools to help those supervising the delivery of drug abuse treatment services to gain insights about personal strengths and weaknesses, and to help guide them to improved leadership and management practices.

   b. Organizational change tools: Handbooks describing step-by-step way to introduce more efficient business practices such as quality management/monitoring, creating empowered work teams, formalized goal setting, improved customer relations, forming organization linkages, and adopting new fiscal and resource management techniques.

   c. Organizational change tools: Handbooks describing step-by-step ways to introduce more efficient or effective therapeutic practices such as, adding pharmacotherapy in a previously drug-free clinic, adopting new medical/pharmacotherapy or behavioral interventions, and adopting new approaches to clinical collaboration and/or case management.

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5. *Web-Based Technologies: Transporting Services Research to Practice*. This initiative will support the development and testing of the effectiveness of web-based technologies that facilitate the translation of drug abuse prevention and treatment services research into practice. The ultimate goal is the delivery of efficacious, low-cost interventions to the greatest number of individuals in community settings. Delivery of evidence-based services in community settings often is hampered by lack of state-of-the-art information about the contents of efficacious interventions, the organizational structures and processes that make effective implementation possible, and available training and technical assistance. Applications may include, but are not limited to, the development and testing of new and innovative Internet-based systems that provide practitioners with (a) current information on evidence-based treatments with the greatest promise for defined populations of drug abusers; (b) assistance in translating clinical trials data into clinically useful information; (c) information and training on how to effectively organize, manage, and deliver evidence-based prevention and treatment services; (d) strategies for organizational change and capacity building; and (e) access to training and technical assistance on the adoption of new prevention and treatment interventions.

6. *New Technologies for Screening, Assessing, and Preventing Problem Drug Use and Matching Patients with Appropriate Treatment Services.* Increased understanding of the complexities of problem drug use has sparked growing interest in and increased need for new user-friendly technologies to assist in the screening, assessment, and prevention of drug abuse and in the matching of patients with appropriate treatment services. New technologies, including CD-ROM, hand-held, Internet, videotape, videodisc, and other electronic means have great potential for helping treatment providers in specialty and non-specialty care settings including primary care contexts to (a) screen for problem drug use and associated health problems and risk behaviors, (b) assess the nature and degree of drug use, (c) embed items for screening or assessing problem drug use within existing clinical tools, (d) deliver appropriate prevention interventions, and (e) identify appropriate types and levels of treatment services for patients based on their individual treatment needs. These new technologies potentially can provide a more cost effective way of identifying problem drug use and associated health problems in a variety of health care settings, speeding the assessment process, preventing the escalation of use to abuse, and improving treatment placement decisions.

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7. *Reintegration of Criminal Offenders into the Community.* Many offenders enter the criminal justice system with drug abuse problems and related health issues. In addition to addressing these health care issues within the prison walls, treatment programs are increasingly called upon to help offenders successfully reintegrate into the community following incarceration. This often means helping offenders to manage their recovery through monitoring, linkage with continuing care services, development of social support networks, and education of friends and family members about the nature of drug abuse and the challenges facing the offender upon release from prison. It is estimated that over the next several years, more than 600,000 criminal justice offenders, many of whom have drug abuse problems, per year will be released to return to their communities. New technologies are needed to help treatment providers in the criminal justice system and in the community coordinate efforts to effectively (a) monitor offenders' recovery once they have been released into the community, (b) prevent relapse, (c) identify relapse early and efficiently re-engage released offenders in appropriate treatment, (d) link released offenders with continuing care services in the community, (e) develop social support networks for recently released offenders in recovery, and (e) educate offenders' family members so that they can more effectively support offenders in recovery once they have been released from prison.

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Office of Science Policy and Communications (OSPC)

Science Education. In order to improve science education in the area of drug abuse research (e.g., disciplines such as neuroscience, psychology, epidemiology), efforts are needed to develop innovative methods for improving knowledge of and generating interest in science among school children, the general public, and health care providers, including providers involved in drug abuse treatment. These might include but are not limited to:

a. Development of methodologies to present drug abuse and science information to particular groups, such as kindergarten and elementary school students, African Americans, Hispanics, persons with disabilities and health care providers.

b. Development of methodology to transfer new knowledge and directions of scientific growth to teachers, curriculum developers and health care providers.

c. Development of computer based learning systems that allow students to experience the scientific process.

d. Development of specific materials, activities, or programs that promote science education related to drug abuse, such as exhibits, curriculum materials, coloring books, videos,

teacher education workshops, partnership programs with scientists and educators, or workshops for health care providers.

e. Development of specific materials, activities or programs that promote the teaching of scientific and research ethics to middle and high school students.

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International Program

NIDA's International Program develops and disseminates important new information on the causes, consequences, prevention and treatment of drug abuse and addiction that will help address the growing problems related to illegal drug use and addiction around the world.

NIDA's International Program is currently interested in supporting US-based small businesses to develop products and services in the following areas:

1. To date opportunities for collaborators to meet have been through an intermediary or sometimes chance meetings. Efforts are needed to use state of the art computer technologies to assist researchers in forming collaborations to further research opportunities.
2. Use of state of the art computer technologies to provide grant writing and other research education skills to US and international audiences.
3. Development of accurate translations of valid and reliable questionnaires, surveys, interviews, and other instruments for use in domestic and international settings.
4. To facilitate research collaborations between US and international researchers, and to respond to the demand for science based drug abuse information, there is a need for the development of a series of information and training modules specially targeted to foreign trainees and investigators. Proposed topics for the modules include, but are not limited to: Drug Abuse Treatment Approaches, Understanding the Neuroscience of Addiction, Tools and Guidelines for Assessing and Evaluating Drug Abuse Treatment Programs and Treatment Approaches with HIV-Positive Drug Abusers.

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Other Research Topic(s) Within the Mission of the Institute

NIDA encourages applications in other areas of research that may not be listed.

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NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)

The NIDCD supports research on the normal mechanisms of, as well as on diseases and disorders of hearing, balance, smell, taste, voice, speech and language. The Institute also supports research related to disease prevention and health promotion. The NIDCD addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders. The NIDCD also supports efforts to create and refine devices, as well as develop cellular-based applications that may replace or substitute for lost and impaired sensory and communication functions. For more specific information about areas of interest to the NIDCD, please visit our home page at http://www.nidcd.nih.gov/.

Phase II Competing Renewal Awards

The NIDCD will accept Phase II SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require

approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval.

The NIDCD will accept applications for up to two (2) years and up to $750,000 per year in total costs. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Please contact your Program Director or Lynn Luethke (NIDCD SBIR/STTR coordinator) before beginning the process of putting an application together. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIDCD SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

Hearing Program

Research and development related to lost auditory function. Development of new cellular and tissue-based applications, hearing aids, cochlear implants, and other assistive devices (e.g., systems designed to improve access to and to increase utilization of computer and other information technologies, telecommunication devices, alerting systems) for individuals with hearing impairments; development of molecular technologies, including viral and non-viral vectors to enable gene transfer to the inner ear; development of cell type specific markers and probes to examine cell lineage in inner ear regeneration; development of research tools such as software and imaging technologies; development of relevant web or other databases; development of assays (including DNA-based assays), tests and instruments for the screening and diagnosis of hearing impairment, especially in neonates and infants; development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new outcome measures for assessing the efficacy of treatments of hearing disorders; development of new research tools to aid in the study of the auditory system (e.g., imaging techniques, neuroanatomic tracers, electrophysiologic technology, new animal models); development of technologies for the study, diagnosis and treatment of otitis media including non-invasive diagnostics to identify middle ear pathogens, novel antibacterial strategies, and prophylactic anti-microbial strategies.

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Balance/Vestibular Program

Research on balance and vestibular function, including development of tests and treatments for balance disorders. Balance disorders affect a large proportion of the population, particularly the elderly. The vestibular system, with its receptor organs located in the inner ear, plays an important role in maintaining orientation in space, controlling balance while the body is immobile and in motion, and visual fixation of objects during head movement. Emphasis is on research and development of treatments for balance disorders; development of neuroimaging techniques, computational modeling, genetic tools and biochemical markers of disease in the vestibular system; development of clinical tests, instrumentation and software systems to assess balance/vestibular function, including otolithic functions and eye movements associated with the vestibulo-ocular reflex; development of instruments and tests measuring head stability and vestibular function during natural stimulation of the vestibular system including during locomotion; development of perceptual reporting techniques and psychological indices for the clinical assessment of the balance-disordered patient; development of tests and new outcome measures for assessing the efficacy of physical rehabilitative regimens for balance disorders; and development of assistive devices for

balance disorders, including prostheses involving electrical stimulation of the vestibular system.

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Voice, Speech, and Language Programs

Research on voice, speech, and language disorders focuses on determining the nature, causes, treatment and prevention of disorders such as stuttering, spasmodic dysphonia, dysarthria, and aphasia. Emphasis is on research and development of diagnostic measures and intervention strategies for voice, speech, swallowing, and language disorders; development of communication and other assistive devices for individuals with voice, speech, swallowing, and language disorders; identification and development of computer and animal models for research in communication disorders; development of new systems for visual communication by individuals who are deaf or severely hearing impaired; development of new systems of communication for individuals with motor impairment; design and development of diagnostic measures or materials for early identification of speech and language impairment in children; development of tests for the assessment of childhood and adult language impairment in multi-cultural populations; development of assessment measures of sign language abilities; development of improved artificial larynges and tracheoesophageal shunts; development of artificial intelligence computer models that simulate normal and disordered speech and language.

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Taste and Smell Program

The study of the chemical senses of taste and smell will lead to a better understanding of how individuals communicate with their environment and interact socially. Taste and smell perception regulates food consumption and plays an important role in maintaining a nutritious healthy diet. In addition, both the olfactory (smell) and gustatory (taste) systems offer special approaches for understanding fundamental mechanisms of neurogenesis, plasticity and regeneration in the brain. Innovative approaches for obtaining functional expression of mammalian taste or odor receptors in heterologous cells will help determine ligand-receptor specificities and taste and smell quality perception. The olfactory receptor neuron represents a model system for the study of the biological processes related to stem cells. Advances in molecular and cellular biology, biophysics, and biochemistry of the olfactory and gustatory systems are paving the way for improved diagnosis, prevention, and treatment of chemosensory disorders. Research on the development of readily administered diagnostic tools for testing human chemosensory function in population studies, intervention strategies for smell and taste disorders, biosensors and electronic noses for medical and industrial applications, and the development of an inventory of chemicals at exceptional high purity have high priority.

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Other Research Topic(s) Within the Mission of the Institute

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NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)

The NIDCR conducts and fosters research on the etiology, pathogenesis, prevention, diagnosis, and treatment of oral, craniofacial and dental diseases and conditions. For more specific information about areas of interest to the NIDCR, please visit our home page at http://www.nidcr.nih.gov.

Developmental Biology and Mammalian Genetics

Emphasis is on the understanding of the development of tooth and bone, and on the identification of the genetic and environmental contributions to craniofacial disorders. The objective of this scientific program is to elucidate the underlying causes of craniofacial disorders, thereby advancing the fields of diagnosis, treatment, and prevention.

A. Develop and operate registries to track craniofacial birth defects, diagnostic techniques, treatment protocols, and outcome assessments.

B. Develop and manage tissue banks and/or DNA libraries of samples from patients with craniofacial birth defects and from unaffected relatives to aid in prospective and retrospective epidemiology and linkage studies to facilitate the discovery of genes involved in craniofacial dysmorphologies.

C. Production of genetic and immunological markers specific for developing craniofacial tissues (e.g., stage specific markers for discreet populations of premigratory, migratory, and differentiating neural crest cells).

D. Develop early pregnancy genetic tests to screen fetal cells in maternal blood for genetic mutations involved in inherited syndrome and non-syndrome craniofacial defects.

E. Develop instrumentation to improve the diagnosis and treatment of inherited and acquired craniofacial defects.

F. Develop instrumentation and methods to more accurately measure craniofacial growth in order to assess normal growth patterns as well as the effects of treatment procedures.

G. Develop animal models possessing specific genetic craniofacial anomalies for use in studies on the etiology of disease, gene regulation, gene/environment analysis, and gene-product function and development of treatment protocols.

H. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

Infectious Diseases and Immunity

Research relating to the etiology, pathogenesis, prevention, diagnosis and treatment of infectious diseases of the oral cavity is supported by the NIDCR. This includes research on practical ways to effectively use the host immune system to prevent or treat oral infectious diseases and microbial-induced inflammation. Infectious diseases of the oral cavity include caries, periodontitis, candidiasis, peri-implantitis, pulpitis, and various viral and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations of HIV infection and AIDS.

A. Develop improved instrumentation, methodology, biomarkers or molecular probes for the rapid diagnosis and measurement of infectious diseases.

B. Develop diagnostic tests to determine host susceptibility to oral infections.

C. Develop ways to overcome or eliminate the risk of oral infections in persons who smoke or chew tobacco, drink alcohol, or are immunosuppressed, have diabetes, are malnourished, or are psychologically stressed.

D. Explore novel methods or agents to eradicate oral biofilms (dental plaque) on teeth, oral soft tissues, and dental implants without adversely effecting the normal oral flora.

E. Isolate, synthesize or prepare new antibiotics and antimicrobial agents that can overcome bacterial and fungal resistance to current compounds. Formulate combinatorial drug regimens to attack microbes growing in oral biofilms (dental plaque).

F. Develop controlled release drug delivery systems for the prevention and control of oral infectious diseases.

G. Develop biological response modifiers or other immunological approaches to reduce or eliminate microbial-induced chronic inflammation or the tissue destruction associated with chronic inflammation in the oral cavity.

H. Develop improved animal or in vitro models of oral infectious diseases to enable evaluation of pathogenesis and therapies.

I. Develop ways to interfere with microbial colonization and growth through the use of antimicrobial agents and chemotherapy.

J. Establish needed services that will benefit oral health care providers or research laboratories involved in the study or treatment of oral infectious diseases. Such services might be facilities for: software design; design and preparation of peptides and molecular probes; establishing and culturing hybridomas; determining antimicrobial sensitivity of microbes growing in biofilms (dental plaque) to drugs and antibiotics; or high technology imaging.

K. Establish practical methods to increase host immune and non-immune defenses against infectious diseases (e.g., vaccines, biological response modifiers). Develop adjuvants to stimulate mucosal immunity. Identify and characterize target antigens for favoring secretory antibody production.

L. Identify and exploit the structural features of oral biofilms for increased therapeutics delivery.

M. Develop methods for early diagnosis of oral opportunistic infections in asymptomatic individuals exposed to HIV.

N. Develop diagnostic tests utilizing whole saliva and oral biopsies for examination of local immune responses and for the assessment of disease progression.

O. Develop computer programs to model biologically active peptide regions of oral components that have anti-fungal, anti-bacterial and anti-viral activities.

P. Develop substitutes of naturally occurring chemicals (phytochemicals) known to have a role in controlling opportunistic infections induced by HIV.

Q. Develop synthetic peptides and recombinant proteins of oral components with anti-fungal, anti-bacterial and anti-viral, specifically HIV, activities.

R. Develop controlled release delivery systems for local delivery of synthetic peptides recombinant proteins with anti-fungal, anti-bacterial and anti-HIV activities and of drugs.

S. Develop and/or improve innovative and highly sensitive molecular techniques to examine changes of cytokines and other immune regulators, and of viral load in oral tissues and fluids.

Epithelial Cell Regulation and Transformation

Emphasis is on the molecular mechanisms of oral epithelial cell regulation and aberrations of these mechanisms as they relate to the development and progression of diseases involving the oral mucosa including oral neoplasias research related to early diagnosis, prevention, and treatment of oral neoplasias.

A. Develop immunological methods, imaging techniques or genetic markers for the early detection, diagnosis and prognosis of pre-malignant head and neck lesions including oral carcinomas.

B. Develop methods for the rapid and specific detection of viruses implicated in the etiology of oral cancer as well as the detection of viral genes in pre-malignant and malignant head and neck lesions.

C. Develop immunotherapies (e.g. vaccines, gene therapies) effective against viruses suspected to be etiologic agents in the induction of pre-malignant and malignant head and neck lesions.

D. Develop novel techniques for the evaluation of chromosomal changes in head and neck cancers.

E. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant head and neck lesions.

F. Develop novel technologies for the genetic and molecular-targeted therapy of head and neck carcinomas.

G. Develop animal models of localized and metastatic head and neck squamous cell carcinomas.

H. Develop novel genomic and proteomic, as well as micro and nano-sensor technologies, that can aid in early detection of head and neck tumors and can release therapeutic agents in tumor cells.

I. Develop regimens for the alleviation of the oral complications of cancer therapy.

J. Develop novel technologies for using stem cells as therapeutics for head and neck cancers.

Mineralized Tissue and Salivary Gland Physiology, Pharmacogenetics and Injury

Emphasis is on the physiology of bones, teeth and salivary glands, craniofacial tissue damage and repair, and pharmacogenetics of agents used for the treatment of craniofacial and oral diseases and disorders.

A. Develop standardized and more sensitive methods, instrumentation, and/or devices to detect oral bone loss, assess alveolar bone quality, and to monitor for bone repair.

B. Develop novel agents and vehicles for local inhibition of bone loss and/or augmentation of bone growth for the treatment of periodontal diseases or craniofacial reconstruction.

C. Develop better methods and instrumentation to detect and/or treat the earliest signs of demineralized enamel that may develop into carious lesions.

D. Develop novel methods and agents to promote scarless repair of cleft lip and scarless cutaneous healing following craniofacial surgery.

E. Develop viral and non-viral vectors for salivary gene therapy and gene therapeutics.

F. Develop non-invasive methods for the determination of the efficacy and safety of artificial saliva, sialogogues and of their delivery vehicles.

G. Develop apparatus for craniofacial bone distraction that is contained entirely within the oral cavity.

H. Develop more efficient methods, materials, and devices for prevention of injuries to the teeth, mouth, and face during athletic activities.

I. Develop diagnostic reagents and tests necessary to effectively use changes in saliva to diagnose and monitor systemic health, specific disease processes, drug therapy, genetic defects, nutritional status, and age-specific therapy.

J. Develop and characterize immortalized normal human and animal salivary gland epithelial cell lines with appropriate phenotypic expression.

K. Develop genetic standards and diagnostics to predict an individual's oral responses to drug treatment of responsiveness to drugs used for the treatment of craniofacial, oral and dental diseases.

Molecular and Cellular Neuroscience

Emphasis is on research on chronic disabling diseases of the oral-craniofacial-dental areas including chronic pain, neuropathies and neurodegenerative disorders, diseases of the temporomandibular joint.

A. Develop improved techniques for measuring chemosensory, tactile, kinesthetic, or proprioceptive function involving craniofacial structures. Such measures may be useful in screening for deficits, improving diagnosis, or for evaluating responses to dental treatments or interventions.

B. Develop improved measures for assessing oral-motor coordination or oral behaviors (e.g., swallowing, masticatory efficiency).

C. Develop improved biomarkers or treatments for neuropathic conditions or neurodegenerative conditions affecting oral-craniofacial tissues or structures.

D. Develop assays facilitating reliable evaluations of relationships between hormonal or chronobiological variations and other risk factors as these relate to onset or exacerbation of pain symptoms.

E. Develop improved in vitro or animal models for evaluating biomechanical, wear, functional or systemic responses associated with TMJ devices or engineered tissues.

F. Develop improved in vitro or animal models for assessing pathobiological changes in the TMJ or masticatory muscles and improved biochemical markers of joint degradation.

G. Develop innovative approaches to reduce foreign body reactions or to improve surgical outcomes for prosthetic devices or bone grafts received subsequent to failed alloplastic TMJ implants

H. Develop safe and effective biomaterials or procedures useful in repairing the temporomandibular joint (TMJ) following trauma, degenerative or inflammatory diseases processes, or iatrogenically-induced pathology (e.g., failed TMJ implants).

I. Develop more efficient methods, materials, and appliances for orthodontic tooth movement.

J. Discover and develop non-narcotic medications with particular emphasis on chronic orofacial pain disorders.

Biotechnology and Biomaterials

Emphasis is on the development of natural and synthetic materials to be used for the repair, regeneration, restoration and reconstruction of oral tissues and organs; on the development and improvement of evaluation and measurement systems for the characterization of implanted material properties; on their interactions as well as on their performance under the conditions of the biological environment; and finally on the development and/or improvement of new dental restorative materials that are mercury free.

A. Develop strategies for the fabrication of site-specific repair and regeneration systems (e.g., smart implants to specifically attach the appropriate reparative cells).

B. Establish libraries of structural recognition epitopes (peptides, carbohydrates) to screen biological activities (e.g., bacterial adherence to soft and hard oral tissues).

C. Develop non-destructive methods for the characterization of material properties in vivo and in vitro.

D. Develop synthetic analogues of oral/craniofacial tissues and organs.

E. Develop more sensitive methods to determine and measure the interactions of materials with biological systems (e.g., material biocompatibility and bioactivity in the oral environment).

F. Optimize imaging techniques for describing the architecture of oral tissues and structures.

G. Develop computer and mathematical modeling systems capable of mimicking biological tissues and of evaluating material designs.

H. Develop novel techniques for ensuring sterility of biomimetic structures prior to implantation.

I. Develop delivery systems that are compatible with host immunity; consider hybrids and artificial vectors as well as viral and non-viral gene delivery systems with cell-type selectivity.

J. Develop in vitro methods that predict immunogenicity to vectors used for gene transfer as well as for biomaterials.

K. Develop improved implantable materials, designs through nanotechnology principles.

L. Develop improved surgical techniques for artificial implants to support replacement of dental, oral and craniofacial tissues and organs.

M. Develop new and improved instruments and techniques for the diagnosis and treatment of TMJDs.

N. Develop improved composite materials and adhesive sealants suitable for restoring crowns of posterior teeth and exposed roots of teeth.

O. Utilize nanoscience and nanotechnology principles in the development of new non-mercury containing dental restorative materials.

P. Design and development of orthodontic and other prosthetic appliances.

Q. Develop tissue engineering and regenerative approaches to building complex structures (e.g. teeth, ligaments, peridontum) in the oral cavity.

Clinical, Epidemiological, and Behavioral Research

Provides support for clinical trials and patient-oriented research on the safety, efficacy, and effectiveness of measures for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders, as well as for research on the distribution of such disorders, risk and protective factors, oral health disparities, and basic and applied behavioral, social science and health services research relevant to oral diseases and their prevention or treatment.

A. Develop and test web-based training or other innovative approaches to accelerate accurate translation of new knowledge regarding oral diseases and their effective prevention/treatment into clinical or public health practice.

B. Conduct studies to expand knowledge regarding specific oral health consequences of using various smoked or smokeless tobacco products.

C. Develop reliable, sensitive, cost-effective measures for improved assessment of oral health status in populations or population subgroups.

D. Develop and test the effectiveness of innovative teaching tools to inform oral health

professionals or the public regarding oral cancer prevention and early detection.

E. Develop and test devices or methods to improve time-sampled monitoring of behavioral adherence with preventive or therapeutic regimens specifically relevant to oral diseases/conditions. Such devices or methods could be utilized either within clinical trials or oral health care delivery systems.

F. Develop novel compliance and survey tools to examine the underlying causes of avoidance of preventive dentistry in underserved populations.

Other Research Topic(s) Within the Mission of the Institute

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NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

The NIDDK supports research in diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic and hematologic diseases. For additional information about areas of interest to the NIDDK, please visit our home page at http://www.niddk.nih.gov.

Phase II Competing Renewal Awards

NIDDK will accept Phase II SBIR/STTR Competing Renewal grant applications to continue the process of developing products that ultimately require 1) clinical evaluation, 2) approval by a Federal regulatory agency, and 3) continuing refinements to durable medical equipment (DME) designs such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Such products include, but are not limited to biological products, devices, drugs, medical implants, etc. related to the mission of the NIDDK. The previously funded Phase II SBIR/STTR grant need not have been submitted in response to a particular solicitation, as long as the research is appropriate to the purpose of this solicitation. Budgets up to $1,000,000 total costs per year and time periods up to 3 years may be requested for this Phase II Competing Renewal opportunity. An applicant must provide evidence that they have contacted the Food and Drug Administration (FDA) for guidance concerning the development of a drug, biologic, or medical device. Such evidence should include FDA correspondence regarding an investigational new drug (IND) application, investigational device exemption (IDE), or pre-market notification (510k) for the applicant's product development and the status of their project in a timeline related to Federal regulatory approval processes.

Prospective applicants are strongly encouraged to contact NIH staff listed at the end of this NIDDK topics announcement prior to submission of a Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it

contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities.

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants.
- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.
- Assessment of devices with regard to performance standards related to the FDA approval process.
- Safety and effectiveness studies of novel medical devices and tissue engineered products.
- Biocompatibility studies of surface materials of putative medical implants.
- Evaluation of novel imaging approaches for diagnostic purposes.
- Clinical studies in support of New Drug Application approval by the FDA.
- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Diabetes, Endocrinology and Metabolic Diseases

The Division of Diabetes, Endocrinology and Metabolic Diseases supports basic and clinical research on the etiology, pathogenesis, prevention, diagnosis, and treatment of diabetes mellitus and its complications; endocrine diseases; osteoporosis; cystic fibrosis, and other metabolic disorders; as well as research on basic endocrine and metabolic processes. Research topics of potential interest to small businesses include, but are not limited to:

I. SENSORS AND DELIVERY DEVICES:

A. Assessment of non-invasive, minimally invasive or implantable sensors for monitoring blood or interstitial fluid glucose for prevention of hypo- and hyperglycemia in diabetic patients.

B. Integration of glucose sensor and insulin delivery systems to create an artificial pancreas.

C. Development of improved insulin delivery methods or devices.

D. Development of improved methods to assess and monitor metabolic control.

II. SCREENING TESTS, DIAGNOSTICS AND BIOLOGIC TOOLS:

A. Development of techniques or products useful for predicting, preventing or delaying progression of diabetes and its complications, including tests for identifying patients at risk, and methods of monitoring disease progression.

B. Development of high throughput assays based on biologic pathways likely involved in the pathogenesis of diabetes and its complications that could be used to screen molecular libraries for novel therapeutic agents.

C. Development and validation of animal models or surrogate markers to monitor disease progression and potential therapies for diabetic complications.

D. Development of strategies or tools to support the application of behavioral approaches to risk reduction in the development of type 2 diabetes or to the improved treatment of diabetes. An important consideration should be cost and practicability of use.

E. Development and validation of tools for use by health care providers/systems to improve diabetes care and prevention.

F. Development of techniques and tools to identify islet cell progenitors, methods to predict transplant success with recovered islet preparations, and non-invasive imaging as well as other methods for the *in vivo* measurement/ evaluation of pancreatic beta cell mass, function or inflammation after transplantation of pancreatic islet/beta cells.

G. Development or improvement in diagnostic or screening tests for cystic fibrosis.

H. Identification of new ligands for previously unclassified (orphan) nuclear receptors and development of partial agonists or antagonists with therapeutic potential for diseases such as diabetes and osteoporosis, hormone-dependent cancers, and for conditions such as obesity.

I. Development of Selective Receptor Modulators (SRMs) with tissue specificity and profiles that provide beneficial effects without side effects obtained from therapies based on naturally occurring hormones.

J. Development of simple inexpensive test for diagnosis of diabetes and pre-diabetes that do not require fasting or timed blood sampling.

III. Interventions and Therapies:

Diabetes

A. Development of immunomodulation/tolerance induction strategies to prevent or slow progression of type 1 diabetes.

B. Development of new therapies to prevent, delay or treat diabetes or its complications including strategies or tools to apply behavioral approaches.

C. Development of methods that protect islet grafts after transplantation, including the evaluation of alternative transplantation sites, minimize the use of immunosuppression through immunomodulation/tolerance induction or immunoisolation/encapsulation of the graft from the host immune system, or support the use of single donors for transplantation.

D. Development of methods that expand the number of human islets during culture while still retaining appropriate functional islet characteristics and the ability to be successfully transplanted.

E. Development of methods utilizing replenishable cell sources, especially stem cells that produce functional islet like cells/tissues that can be successfully transplanted.

F. Development of more reproducible methods that improve yield/viability/function of islets prior to transplantation and the engraftment and long term function of islets after transplantation.

Cystic Fibrosis and Inborn Errors

G. Development of potential therapeutics for CF including agents to improve trafficking and function of mutant CFTR, to enhance activities of channels which can serve as alternatives to CFTR, and to increase transcription or translation of CFTR RNA.

H. Production of stabilized biologically active proteins or peptides useful for enzyme replacement therapy.

I. Development of products useful in assessing or improving nutritional status in patients with CF including improved pancreatic enzyme preparations.

IV. Genetic Testing and Genetic Therapies

A. Development of improved methods for the diagnostic, population or newborn screening or prenatal testing for genetic metabolic diseases.

B. Improvements in the construction of gene therapy vectors to increase transduction efficiency, level and duration of expression, and to improve targeting.

C. Development of improved methods of manufacturing gene therapy vectors that are scalable and improve titer and bioactivity of the vectors.

D. Development of new vector systems that improve the ability to transduce nondividing cells such as hematopoietic stem cells, neurons, hepatocytes or epithelial cells.

E. Development of techniques to achieve efficient homologous integration or site-specific integration of introduced genes.

F. Development of approaches to gene transfer for cystic fibrosis by improving gene delivery systems, improving tropism for target cells, increasing efficiency and duration of transgene expression and minimizing toxic effects.

V. Application of Proteomics and Metabolomics to Diabetes, its Complications, and Other Endocrine and Metabolic Diseases

A. Identification of surrogate markers looking at the plasma/sera proteome or metabolome at different stages of diabetes its complications or other endocrine or metabolic diseases.

B. Development of novel proteomic or metabolomic technologies designed to study diabetes its complications or other endocrine or metabolic diseases.

C. Identification of novel drug targets or novel therapeutic agents using proteomic approaches

that might be relevant to diabetes its complications or other endocrine or metabolic diseases.

D. Use of high throughput proteomic and metabolomic technologies for toxicology studies of drugs that might be relevant to diabetes its complications or other endocrine or metabolic diseases.

Digestive Diseases and Nutrition

The Division of Digestive Diseases and Nutrition supports research on the function, diseases and disorders of the digestive tract; the esophagus, stomach, intestine, colon, anorectum, pancreas, liver, gallbladder, and biliary tract; basic, clinical and behavioral research on nutrition and obesity as well as information transfer in the field of digestive diseases and prevention of obesity. Innovative investigator-initiated projects that are not mentioned below are encouraged. Areas that may be of interest to small businesses include, but are not limited to:

I. DIGESTIVE AND LIVER DISEASES (CLINICAL)

A. Development of assays to detect biomarkers for genetic predisposition to GI-relevant diseases, e.g., IBD and IBS.

B. Development of new genetic screening methods for detection of inherited digestive and nutritional disorders, e.g., hemochromatosis, Wilson's disease, Crigler-Najjar syndrome, Alagille syndrome.

C. Development of improved means for detecting Barrett's esophagus.

D. Development of a non-invasive means of localizing GI bleeding beyond the duodenum that is more sensitive than the Tc-RBC test.

E. Development of methods for gastrointestinal endoscopy without the need for sedation.

F. Development, using rational drug design techniques, of agents that interact with L-type calcium channels or with delayed rectifying potassium channels to treat motility disorders (pseudo-obstructive disorder, chronic constipation, and slow bowel transit).

G. Development of pharmaceutics from herbal preparations of promise for therapy of digestive diseases, including liver diseases, involving isolation of active components, preparation of pharmacologically pure preparations, and testing for pharmacokinetics and activity in humans.

H. Development of novel antifibrotic therapies for progressive liver failure.

I. Development of agents that would protect the gut epithelium from the damage caused by chemotherapeutic agents.

J. Development of tests of hepatic "reserve" which would be of use, for example, in assessing the risk of surgery in patients with liver disease.

K. Development of agents to promote the repair of gut epithelium barrier function, e.g., as needed following chemotherapy.

L. Development of drugs for dissolving gallstones in vivo.

M. Development of humanized monoclonal antibodies against HCV and HBV to be used for prevention of recurrent disease in liver transplant patients.

N. Development of surrogate markers for liver fibrosis and progression.

O. Development of a rapid, non-invasive diagnostic test for biliary atresia.

II. DIGESTIVE AND LIVER DISEASES (BASIC)

A. Development of detection methods for non-culturable forms of gut enteric bacteria.

B. Development of molecular probes for the diagnosis of mucosal dysplasia in inflammatory bowel disease.

C. Development of gut immune-modulators, or non-antigenic gliadin in celiac disease.

D. Development of new techniques, including non-invasive imaging, to measure motility/intestinal transit at various sites within the gastrointestinal tract.

E. Development of techniques for the preservation and transplantation of small intestine and pancreas.

F. Development of non-invasive measures of pancreatic exocrine function.

G. Development of a test for determining the hepatotoxic potential of drugs, agents or additives that is more sensitive than testing in mice and reflects the human response to the test compound.

H. Development of animal models to study hepatotoxic agents.

I. Improvements to existing imaging systems, or development of new ones, to allow non-invasive detection of fibrotic, necrotic, inflamed, and fatty livers prior to transplantation.

J. Development of non-invasive techniques to detect liver disease.

K. Development of non-invasive imaging methods to assess fatty liver in patients.

L. Development of non-invasive devices/ techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.

M. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

N. Development of non-occluding stents for use in the biliary tract and in transjugular intra-hepatic porto-systemic shunts (TIPS).

O. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.

P. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.

Q. Development of molecular standards for Hepatitis C virus quantitation and typing.

R. Development of molecular standards for Hepatitis B virus quantitation and typing.

S. Development of an economical, accurate, and fast test for glutens and glidins in foods.

T. Development of humanized mouse models of multi-allelic diseases.

U. Development of measurements to quantitate phenotypic or metabolic markers of disease progression in animal models, thus reducing the numbers of animals needed.

III. Nutrition

A. Development of a better method for measuring food intake patterns of individuals that could replace recall.

B. Development of better methods for assessing overall nutritional status.

C. Development of a non-invasive breath or blood test to accurately measure dietary fat intake.

D. Development of biological measures, such as serum or urine tests, for long-term dietary consumption of specific nutrients.

E. Development of better means of assessing energy intake and/or energy expenditure (i.e., physical activity), e.g., a device to estimate movement and relate this to calories expended with the goal of impacting behavior and preventing obesity.

F. Development of better means to detect food borne pathogens with the goals of (1) preventing their inclusion in foodstuffs and (2) better treatment of acute infections.

IV. Obesity and Eating Disorders

A. Development of safe drugs or herbal products that inhibit appetite or increase energy expenditure.

B. Development of computerized interventions for weight-loss/maintenance and/or increasing physical activity such as hand-held computers and web-based programs.

C. Development of devices/equipment/ interventions to encourage “activity” while performing sedentary work.

D. New technologies for quantitative assessment of intra-abdominal fat; emphasis on technologies that are non-invasive, minimize the use of ionizing radiation, and have the capability of being adapted for use in the usual health care settings.

E. Development of more economical methods to produce 18-labelled oxygen for use in energy expenditure studies and/or body composition studies using doubly labeled water.

Kidney, Urologic and Hematologic Diseases

The Division of Kidney, Urologic, and Hematologic Diseases supports research into basic mechanisms of organ and tissue function and into the diseases of the kidney, urologic and hematologic systems. Projects to help develop an understanding of the physiology, pathophysiology, and related diseases of the kidney, urinary tract, and blood and blood forming systems so that rational treatments and means of prevention and/or arrest of diseases may be devised. Support for advances in the technology of cell and molecular biology that will enhance

research in kidney, urologic and hematologic diseases is encouraged. Research opportunities of interest to small businesses include, but are not limited to:

I. Development of a Genomic Toolbox for Study of Kidney, Prostate, Bladder, or Red Cells, which would include:

A. Library generation and gene identification from whole organ or rare compartments in normal, developing, or injured tissues.

B. Antibodies or phage libraries that will facilitate the prospective identification and purification of renal cell types.

C. Strategies to deal with the anatomical complexity, increase the representation of low abundance transcripts, or decrease the redundant sequencing of over-represented or known genes.

D. Bioinformatic tools.

E. Flexible databases useful for designing organ-specific databases and websites.

F. Techniques for visualizing RNA distribution within cells or tissues.

G. New methods to acquire material from archival samples.

II. Kidney

A. Development of antibodies or phage libraries specific for the individual cell types of the kidney.

B. Development of both data and cell banks of diabetic kidney disease families and autosomal and recessive polycystic disease families for use by the research community.

C. Development of pharmacological agents that might be used to intervene in acute or chronic renal disorders and in disorders of renal hemodynamics, blood pressure, and extracellular volume regulation.

D. Means to improve physiologic homeostasis in maintenance dialysis therapy through the:

1. Improvement of blood access to permit continuous access to the circulation.
2. Development of means to provide for continuous anticoagulation.
3. Development of reliable, non-invasive, online hemodialysis monitoring systems assessing real-time treatment parameters such as blood volume, access flow, and urea clearance.

E. Studies to improve the efficiency of maintenance dialysis:

1. Development of innovative methods to produce more efficient and less morbid forms of renal dialysis (e.g., GI dialysis, artificial kidney).
2. Studies on biocompatibility of artificial kidney membranes, in surface sensitive proteins, complement, and clotting mechanisms.
3. Development of new agents for sterilizing dialysis membranes.
4. Development of new dialysis membranes to diminish the duration of dialysis treatments.

F. Improved techniques of preservation and storage of kidneys intended for transplantation.

G. Development of material(s) for construction of urinary catheters that may reduce the incidence of infection in the urinary tract.

H. Development of improved renal imaging techniques, differential renal function assessments and diagnostic distinction between benign and malignant parenchymal diseases.

I. Development of early diagnostic tools, preventative measures, and treatment modalities for Acute Renal Failure.

J. Identification of mediators of renal failure during sepsis and pharmacological means to block these effects.

K. Development of new non-invasive methods for measuring kidney function:

1. Reliable, non-invasive, non-radioactive methods of measuring glomerular filtration rate (GFR).
2. Identification and description of physiologic compounds that are filtered by the kidney, but neither secreted or reabsorbed;
3. Identification of serum factors released by damaged kidney cells.
4. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity.

5. Development of new biomarkers for early detection of kidney dysfunction, prediction of progression, and early indication of recovery.
6. Development of rapid, accurate, and cost effective means of quantifying urine albumin.

III. UROLOGY

A. Study of the effect of growth factors, hormonal concentrations and other biochemical stimuli on the growth of prostatic tissue. Analyses of factors responsible for initiation and progression of Benign Prostatic Hyperplasia (BPH).

B. Development of animal or in-vitro models for the study of stromal - epithelial interactions in BPH.

C. Assessment of factors responsible for Benign Prostatic Hyperplasia (BPH) induced uropathy.

D. Host-parasite and bacteria-urothelial cell interactions involved in urinary tract infection.

E. Kinetics of renal stone formation, such as characterization of growth and dissolution, or crystal growth inhibition, and definition of reliable biochemical profiles of stone forming patients.

F. Development of additional therapeutic agents for prevention and/or treatment of urolithiasis.

G. Neuropharmacological-neurophysiological assessments in urodynamics.

H. Development of culture conditions for in vitro culture of cells from benign prostatic hyperplasia.

I. Development of serum or urine markers that correlate with prostate size to evaluate rate of growth.

J. Development of non-invasive instrumentation that can detect early onset of bladder instability associated with diabetes mellitus.

IV. HEMATOLOGY

A. Development of methods and equipment for routine high volume isolation of highly purified hematopoietic stem and progenitor populations.

B. Identification of new methods to assay hematopoietic stem and progenitor cells with short- and long- term repopulation models amenable to serial examination.

C. Development of chemically defined reagents that support hematopoietic stem cell proliferation and differentiation.

D. Definition of culture conditions using serum-free medium that will support the ex vivo expansion of hematopoietic stem and progenitor cells.

E. Development of new approaches for identifying, isolating, and genetically analyzing fetal erythrocytes in the maternal circulation.

F. Development of novel methods for the delivery of DNA, proteins, and other compounds to hematopoietic stem cells.

G. Development of rapid, high throughput microarrays for accurate assessment of gene expression profiles of hematopoietic stem cells.

H. Development of non-invasive systems for monitoring the total hemoglobin and hematocrit, suitable for use with adults or neonates.

I. Application of nanotechnology to the measurement of blood parameters and diagnosis of blood disorders.

J. Development of new methods for the non-invasive or minimally invasive measurement of body iron.

K. Adaptation of MRI technology for the non-invasive measurement of body iron:

1. Develop appropriate MR measurement method(s).
2. Optimize RF coils for the body region of interest (primarily heart, liver, and pancreas).
3. Develop magnets of the appropriate magnetic field strength(s).
4. Develop a reliable method for calibrating and validating iron concentration detected by magnetic resonance imaging.
5. Determine the most appropriate magnetic resonance method for determining relaxation times and susceptibility.
6. Develop indicator materials for direct MR measurement of iron concentration.

L. Design of therapeutic drugs for inducing fetal hemoglobin synthesis.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Human health and human disease result from three interactive elements: environmental exposures, genetic susceptibility and age. The mission of the NIEHS is to reduce the burden of human disease and dysfunction from environmental causes by understanding each of these components and how they interrelate. NIEHS achieves its mission through a multidisciplinary biomedical research program, prevention and intervention efforts, and a communication strategy that encompasses training, education, and technology transfer and community outreach. NIEHS supports research and training focused on the identification, assessment and mechanism of action of agents in the environment and how they contribute to disease and dysfunction. The ultimate goal of these NIEHS activities is to then transfer this knowledge for the public benefit. The

SBIR program uses a combination of research, technology transfer and communication strategies to aid the mission of NIEHS.

For additional information about the areas of interest to NIEHS, visit our home page at http://www.niehs.nih.gov.

Exposure Biology Program

Fundamental to the NIEHS mission is the ability to quantify an individual's exposure, as well as the unique characteristics that account for individualized responses to the exposures. The goal of this exposure biology program is to develop new technology and assays to generate precise measurements of human exposure to chemical and biological agents that may lead to disease or dysfunction. For the purpose of this solicitation the focus of this program will be on respiratory disease or reproduction and development. For example, exposures to microbial toxins, particulates, and ozone may result in a spectrum of respiratory effects ranging from allergic sensitization and immune reactivity to chronic lung disease. Exposures to other environmental agents such as pesticides, phthalates, and polybrominated biphenyl ethers (PBDEs) may result in adverse effects on outcomes of pregnancy and development. The desired application of these technologies and assays is in population-based (epidemiological) or clinical research and practice.

It is anticipated that the new technologies and assays, such as those based on micro- and nanotechnology and molecular imaging, may provide sensitive, high throughput, and potentially portable systems capable of measuring environmental exposures and the impact of the exposures on human biology. Ideally, such technologies and assays will provide exposure measurements with a high degree of temporal and spatial resolution; that is, they will provide real-time measurements of exposure (high temporal resolution) as an individual moves from location to location (high spatial resolution). Additionally, the technologies and assays will be able to provide precise, quantitative measurements of both current (and ongoing) exposures and/or past exposures, depending on the exposure agent measured.

1. TECHNOLOGIES FOR GENERATING PRECISE MEASURES OF ENVIRONMENTAL EXPOSURES

NIEHS is interested in developing and validating new products/devices, tools, assays to improve our ability to precisely measure environmental exposures to individuals with high temporal and spatial resolution. Ideally, the technologies, tools and assays will be of appropriate scale to be field deployable and/or wearable. Exposures of interest are those related to respiratory diseases, adverse effects on reproduction and development as well as bioterrorism agents(nerve agents, choking agents, metabolic poisons and blistering agents). Examples include:

A. Novel technologies and assays to generate precise, quantitative measures of human exposure at the point of contact (e.g., skin, breath, nasal mucosa).

B. Remote sensing technologies for detecting, quantifying, and monitoring household exposures to toxicants and/or bioaerosols.

C. Micro- and nano-scale technologies, such as lab-on-chip sensors, for detecting and quantifying simultaneously multiple environmental exposure agents in a specific chemical or biological class in environmental samples collected in the personal environment (e.g., breathing zone, clothing, household,

D. Field deployable diagnostic devices capable of assaying biomarkers indicative of specific exposures in biological samples encountered in a mass casualty situation.

2. TECHNOLOGIES FOR GENERATING PRECISE MEASURES OF BIOLOGICAL RESPONSE TO ENVIRONMENTAL EXPOSURES

NIEHS is interested in developing technologies and methods to generate precise indicators (or markers) of the biological response to environmental exposures related to respiratory diseases and adverse effects on reproduction and development. The indicators may reflect compensatory biological responses and/or early (preclinical) responses to the exposure agent. The goal is to develop quantitative indicators (or markers) that can be measured non-invasively in human population-based and clinical research and practice. The exposure markers may reflect either acute or chronic responses related to toxicity or preclinical disease. Examples include:

A. Development of high-throughout and sensitive technologies and assays for the detection and quantification of molecular changes in genes, proteins, or metabolites, that are reflective of the early response to environmental exposure,

in samples of blood, urine, saliva, nasal mucosa, fat and other biological samples.

B. Wearable devices for rapid, real-time monitoring of physiological parameters such as heart rate, blood pressure, caloric output, blood oxygen, and blood glucose, which may modulate the response to environmental chemicals and biological agents.

C. Technologies and assays for identifying high-risk individuals for respiratory diseases and adverse effects on reproduction and development based on environmental exposure measures and genetics.

D. Identification of early (preclinical) response markers in animal models that have direct application to marker development and validation in population-based and clinical studies.

E Devices for assessing not only biomarkers of exposure but also distinguishing those exposed individuals at risk of developing life-threatening symptoms or long term chronic sequelae from their exposure.

Hazardous Waste Assessment, Evaluation and Remediation Program

NIEHS is interested in applying biotechnology and bioengineering approaches for the development of novel strategies that can be used to characterize and monitor contaminants at waste sites, and to reduce exposure via remediation technologies. In addition there is interest in developing products for better site characterization that includes improved monitoring capabilities to assess the extent and amount of contaminants present at sites, as well as to monitor the effectiveness of remediation technology in reducing the amount and toxicity of contaminants. Examples include but are not limited to:

A. Development of nano structures, electrochemical methods, photocatalytic processes, thermal treatments or filtration-based methods of remediation.

B. Development of bioremediation and phytoremediation technologies including the use of genetic engineering approaches.

C. Development of model organisms for site characterization that monitor genomic responses to environmental exposures, with a special interest in metals.

D. Development of technologies to determine the extent to which a contaminant is bioavailable .

E. Development of methods/instruments to detect and measure non-aqueous phase liquids and dense non-aqueous phase liquids in the subsurface.

F. Development of instruments to identify subsurface geological structures and hydro-geological configurations and to sample for the presence of contaminants in these structures.

Predictive Test Systems for Safety Evaluation Program

NIEHS is interested in developing, standardizing, and validating sensitive and specific new and novel tests or batteries of tests that will provide faster and less expensive alternatives to the use of standard laboratory animal tests,(i.e., assays for carcinogenicity, immunotoxicity, reproductive or developmental toxicity, dermal toxicity, and neuro or other organ system toxicity including acute local and systemic toxicity). The proposed tests should use cell cultures or animal models that are relevant to human experience and can be extrapolated to estimate risk to humans. The NIEHS is interested in developing both high throughput screens that can be used to prioritize chemicals for definitive testing and in developing specific tests that meet regulatory requirements for toxicity tests. The endpoints for these assays should take advantage of the new technologies such as genomics, transcriptomics, proteomics, and bioinformatics and of novel endpoints (biomarkers) including those that are non-invasive. Examples include but are not limited to:

A. Biokinetic models that include the integration of toxicodynamic and biokinetic modeling to predict systemic toxicity.

B. In vitro test methods (e.g., undifferentiated/ differentiated human/mammalian cell model systems, organotypic model systems) that can be used to predict acute and chronic toxicity by taking into account, for example, metabolism, the ability of chemicals to pass through barriers (i.e., blood brain, kidney, lung, gastrointestinal), and organ specific effects, or which allow the development of endpoints that can be extrapolated to in vivo biomarkers of toxicity.

C. Alternative assays to determine dermal irritation, dermal absorption, dermal hypersensitivity phototoxicity, and ocular toxicity.

D. Non-mammalian or invertebrate models for specific toxicities that utilize endpoint that are conserved across species so the results can be extrapolated to human risk.

Educational and Training Resources Program

NIEHS is interested in developing educational and training resources for students of all ages, educators, health care professionals and the lay community to enhance their knowledge of environmental health sciences. These resources are an important part of our communication strategy that encompasses training, education, and community outreach. Resources may be directed at all levels of education: Kindergarten through 12th grade, undergraduate, graduate, adult education, health care professional training, and community outreach. Products may include:

A. Web-based interactive lessons, training modules and educational games that can be used in the classroom as well as in the home.

B. Innovative communication strategies for distance learning (e.g. satellite broadcasting, video conferencing, webcasting, Personal Digital Assistant programs, etc.) to enhance educational and training opportunities.

C. Video and DVD-based educational outreach materials that can be used in the classroom, at community meetings, or for professional development, including continuing medical education courses.

D. Educational television shows (e.g., PBS Kids, NOVA, etc.) with accompanying lessons or activities (accessible via internet or print) that can be used by teachers, parents or professional development coordinators.

Resources on subjects of particular interest include, risk assessment, hazards in our environment, use of pesticides, endocrine disruptors, air/soil/water quality, susceptibility/gene-environment interactions, ethical, legal, and social implications of environmental health research, health disparities, and intervention/prevention strategies.

Educational and training materials must be aligned with state and federal standards. Training materials and activities for health care professionals should include continuing education units. Partnerships are encouraged among small businesses, environmental health scientists, and educators, health literacy experts or training specialists.

For more information on NIEHS Science Education activities, visit www.niehs.nih.gov/science-education/.

Other Topics Within the Mission of the Institute

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NATIONAL EYE INSTITUTE (NEI)

The NEI supports research with respect to blinding eye diseases, visual disorders, mechanisms of normal visual function, preservation of sight, and the special health problems and requirements of individuals with impaired vision. Proposals for all areas in basic and clinical vision research are encouraged. Some examples are listed below.

With recent advances in genomics and proteomics, the NEI is interested in providing support for the development of new technologies, strategies, research tools, reagents and methods that can be applied to basic and translational research which will benefit vision health.

The NEI's programs are described in extensive detail in documents which are available from the Institute. For additional information about the research programs of the NEI, please visit our home page at http://www.nei.nih.gov.

Retinal Diseases Program

Research and development of new therapeutic approaches for ocular inflammatory diseases and to inhibit abnormal proliferation of the retinal and

choroidal blood vessels; development of better methods of diagnosing and treating diabetic retinopathy and other vascular diseases of the retina and choroid; development of non-invasive techniques for early diagnosis of macular degeneration and other retinal degenerative diseases; development of instruments and procedures for improved surgical management of retinal detachments; identification and characterization of factors regulating retinal cellular proliferation and development that will facilitate retinal regeneration and function.

Corneal Diseases Program

Research and development of new therapeutic agents for the treatment of corneal diseases; development of innovative methods of drug delivery for ocular surface disorders; development of new biomaterials for corneal prostheses; development of instruments and procedures for correcting the refractive power of the cornea and measuring the cornea's optical and physiological properties.

Lens and Cataract Program

Research and development of therapeutic agents for the prevention of cataract; development of new approaches in the post-operative management of cataract surgery; development of new surgical instruments for cataract extraction and biomaterials for replacement of the natural lens.

Glaucoma and Optic Neuropathies Program

Research and development of new therapeutic agents, instruments, and procedures for the diagnosis and treatment of glaucoma; development of non-invasive methods to measure changes in the optic nerve head and retinal fiber layer.

Strabismus, Amblyopia, and Visual Processing Program

Research into the identification and characterization of growth factors which facilitate regeneration of visual nerve axons; development of innovative techniques to study factors that facilitate regeneration and guidance of developing or regenerating nerve fibers; development of new approaches using imaging techniques, such as PET and MRI, to localize lesions and test the functioning of specific parts of the visual system, especially those involved in higher order visual processing and oculomotor processing.

Visual Impairment and Blindness Program

Research and development of instruments and methods to better specify, measure, and categorize residual visual function; development and evaluation of optical, electronic, and other devices that meet the rehabilitative needs of persons who are blind or have low vision.

Other Research Topic(s) Within the Mission of the Institute

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NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

The NIGMS supports research and research training in the basic medical sciences and related natural and behavioral sciences and in specific clinical areas (i.e., clinical pharmacology, trauma and burn injury, and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components. The three divisions and one center that support research of potential interest to small businesses and their collaborators include:

- Division of Cell Biology and Biophysics
- Division of Genetics and Developmental Biology
- Division of Pharmacology, Physiology, and Biological Chemistry
- Center for Bioinformatics and Computational Biology

For additional information about areas of interest to the NIGMS, please visit our home page at http://www.nigms.nih.gov. This site includes staff contact information by program area (http://www.nigms.nih.gov/nigms_staff/contact.html).

It also includes links to program announcements that highlight NIGMS areas of special emphasis (http://www.nigms.nih.gov/funding/funding.html). In some cases, these announcements specifically mention the SBIR and STTR grant mechanisms, in most cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in these announcements.

Division of Cell Biology and Biophysics

Research on membrane synthesis, structure, and function; membrane models; membrane transport; cell division; cell organization; cell motility; and biophysics of proteins, nucleic acids, and biological assemblies, including viral entry, packaging, maturation, and release, as well as the development of instrumentation, components, and methods for the analysis of cellular components and macromolecules by imaging, spectroscopy, and diffraction analysis.

SBIR and STTR proposals on the application of cell biology, biophysics, biochemistry, physics, mathematics, and chemistry to biomedical problems, and the development of instrumentation to facilitate research in cell biology and biophysics, such as, but not limited to, the topics listed below are welcome.

A. Development and improvement of methods for the expression, solubilization, and purification of milligram quantities of regulatory, cellular, and membrane associated proteins, as well as for the preparation of specifically labeled macromolecules and the recovery of proteins from inclusion bodies.

B. Development of novel ligands, inhibitors, and other probes for spectroscopic and microscopic analysis of cellular assemblies and viral structures, macromolecules and components, their localization and function in vivo and at a single molecule level.

C. Development of instrumentation, devices, and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.

D. Development of new methods and materials directed toward the solution of biological macromolecule structures by, but not limited to, x-ray diffraction, electron diffraction, and NMR spectroscopy.

   1. New methods for the determination of the structures of membrane associated proteins.
   2. New methods for the determination of macromolecular structures in a high throughput mode, including improved detectors, data collection, automated data analysis, and faster software for structure calculations and comparisons.
   3. New methods designed to improve the efficiency of beam line use at synchrotrons.

E. Development of technology for the imaging of molecules and cells, including but not limited to:

   1. Reagents, methods, instrumentation and software for existing and potential kinds of microscopy of molecules and cells (including light, electron, X-ray, scanning probe, and others). Improved probes and supporting technologies for dynamic (real-time) imaging of molecules and molecular events in living cells by light microscopy.
   2. Reagents, methods, and software for conventional and cryo-electron microscopy, including automated apparatus for controlled and reproducible specimen preparation.
   3. Instrumentation, methods and technologies for analysis and manipulation of cells, subcellular components, and single molecules, including atomic force microscopy, atomic forceps and tweezers, and solid state microscopy.
   4. Development of analytical systems and tools such as imaging systems and probes, to be used at the nanoscale.
   5. Methods, probes, and data analysis for spectroscopy, including magnetic resonance, fluorescence spectroscopy, and EPR.

F. Bioinformatics, including but not limited to:

   1. Development of databases relative to structural and cellular biology.
   2. Development of methods for linking the information that might be contained in such databases.
   3. Development of new tools that might be used for “mining” the information contained in such databases.

G. Theoretical methods for, but not limited to:

1. Analysis of macromolecular structures.
2. Prediction of the three dimensional structures of biological macromolecules.
3. Improved methods for structure-based drug design.
4. Improved methods for understanding complex systems at the cellular and organism level.

H. Development of computerized tools that might be used in the presentation of the concepts of cell and structural biology to audiences at a variety of levels.

Division of Genetics and Developmental Biology

Research on developing a better understanding of fundamental processes and mechanisms of development and inheritance in health and disease. Support of basic topics in genetics and developmental biology, including nucleic acid chemistry, the structure of genetic material, the mechanisms of transmission and expression of genetic information, cellular regulation of growth and differentiation, molecular immunology, and population genetics. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of computer software for the analysis of the primary and secondary structures of nucleic acids as these relate to genetic problems.

B. Improvement in procedures for the separation and analysis of nucleic acids and proteins as these relate to genetic problems.

C. Improvement of methodology (technology) for genetic analysis (e.g., gene libraries, cloning techniques, probes).

D. Development of probes for detection of human genetic polymorphisms, including disease genes.

E. Development of improved procedures for cytogenetics.

F. Improvement in procedures (statistical, computational, laboratory) for the analysis of gene flow and gene dynamics in human populations.

G. Development of improved vectors for gene transfer.

H. Development of valid animal models for genetic diseases.

I. Development of quantitative approaches to the analysis of complex biological systems.

J. Development of new tools and models for study of the genetic architecture of complex phenotypes.

K. Development of improved technology to scale up the growth of approved human embryonic stem cells in culture and to regulate their differentiation state.

L. Development of markers, reagents and tools to characterize the unique properties of approved human embryonic stem cell lines and to distinguish them from adult stem cells and more differentiated cells.

M. Development of human embryonic stem cell lines as a primary cell type to be used as a model system for drug discovery.

N. Development or improvement of methodology for generation of antibodies or other affinity reagents for proteins and other small molecules in non-mammalian genetic model systems.

O. Development of methods for chemical modifications that improve the properties of nucleic acids for gene silencing.

P. Improvement in procedures (statistical, computational, laboratory) for the high- and medium-throughput analysis of gene expression patterns and regulatory networks.

Division of Pharmacology, Physiology, and Biological Chemistry

Research related to the actions of therapeutics, including anesthetics, and the development of biotechnological methods for their production and investigation. Research on pain management as it relates to anesthesia and the perioperative period. Research on responses to traumatic injury, including burn injury, and methods to mitigate these responses. Research leading to new knowledge of physiological functions at the molecular, cellular, and organ systems levels. Research on the structure, function, and biosynthesis of cellular components and cellular metabolism, bioenergetics, and mechanisms of enzyme action, regulation, and inhibition. Research leading to the synthesis of new materials or development of new chemical methods to probe biological phenomena or to alter the behavior of biological systems. Examples include, but are not limited to:

A. Methods for isolation, characterization, and production of natural and bio-engineered products.

1. Metabolic engineering for the production of biochemicals through genetic and bioengineering manipulation of biosynthetic pathways.
2. Biosensors for use both in vivo and in vitro in process engineering.

B. Development of innovative synthetic chemistry.

1. Catalytic asymmetric methods and methods for large-scale synthesis.
2. New methods applicable to combinatorial library construction, design, analysis, and/or handling.
3. Improved methods for preparation of isotopically labeled amino acids, peptides, proteins, and prosthetic groups, and therapeutic agents.

C. Development of enzymes, catalytic antibodies, ribozymes, artificial enzymes, and host molecules as drugs or synthetic tools.

1. Synthesis of suicide substrates, affinity labeling agents, and transition state analogs as potential therapeutic agents.
2. New enzyme assays to reduce the reliance on radio-isotopes.
3. General approaches for high throughput screening.

D. Isolation, characterization, and development of factors involved in tissue repair and wound healing, i.e., growth factors. Tissue engineering. Development of artificial skin and skin replacements.

E. Improved systems for collection, processing, and analysis of real time physiological data from injured or critically ill patients. Application of artificial intelligence or fuzzy logic and other methods to model non-linear behavior in critically ill patients.

F. Systems to utilize virtual reality for surgical education and remote surgical applications.

G. Research to improve drug design.

1. Methods for understanding of structure-activity relationships.
2. Mechanisms of drug-receptor interactions.
3. Development of pro-drug and drug delivery strategies.
4. Development of molecular diversity libraries.

H. Research to improve drug bioavailability by improved understanding of factors that influence absorption, metabolism, transport, or clearance of therapeutics and underlying mechanisms.

1. Determination of structure-activity relationships for drug metabolizing enzymes.
2. Determination of structure-transport relationships for active and passive transport of drugs and metabolites.
3. Research on drug transporter structure, function, and regulation.
4. Development and validation of models for prediction of drug bioavailability and metabolism in humans.
5. Research on inter- and intra-individual differences in bioavailability.
6. Methods to improve sensitivity, accuracy, speed, and simplicity for measurements of drugs and their metabolites in complex biological matrices.

I. Application of pharmacokinetic and pharmaceutical principles to the study of large biomolecules, such as proteins, polypeptides, and oligonucleotides.

J. Development of novel targeted delivery systems for both conventional drugs and large molecules.

K. Research to discover, detect, and understand the genetic basis of interindividual differences in drug responses.

1. Identification of human polymorphisms in drug receptor and drug metabolizing enzymes.
2. Methods for pharmacogenetic and pharmacogenomic analyses and their application to phenotypic and genotypic characterization of populations.
3. Development of proteomic and metabolomic methodologies to support research in this area.

4. Development of appropriate databases, specimen, and cell culture collections to support research in this area.

L. Development of novel in vivo and in vitro methods to predict toxicities of pharmacologic agents.

M. Development of differentiated hepatic cell lines from human stem cells that are equivalent to adult hepatocytes to characterize metabolic profiles of pharmacological candidates by phase 1 and 2 enzymes.

N. Development of bioinformatic resources and/or pharmacokinetic modeling programs which utilize ADME parameters of drugs and pharmacogenomic information of individual patients or patient populations to reduce adverse drug reactions in individual patients.

O. Development of methods for quantitating protein and lipid glycoconjugates and for determining their structures. Development of generally applicable methods for the synthesis of branched chain oligosaccharides.

P. Development and application of methods and materials for the elucidation of membrane protein structures at or near atomic resolution.

1. Novel vector and host cell systems for over-expression of membrane proteins, in both unlabeled and isotopically labeled forms.
2. Novel and high purity detergents and non-detergent solubilization agents for the purification and crystallization of membrane proteins.
3. Apparatus to facilitate crystallization and manipulation of fragile crystals for data collection.
4. Reagents for heavy atom derivatization of membrane protein crystals.

Q. Development of high-throughput methods for sequencing and resequencing of mitochondrial genes and relevant nuclear genes and for proteomic profiling of mitochondria in diagnosis of mitochondrial diseases.

R. Development of methods to create site-directed and knock-out mutations of mitochondrially-encoded genes in higher eukaryotic cells and experimental animals.

S. Development of new metal ion chelators and other tools to probe and/or alter the localization and concentration of metal ions in cells and in whole organisms. Research to exploit metal metabolism and metal-regulated cellular control and cell-cell signaling processes to probe and/or alter cell function. Research to develop investigational and therapeutic applications of metal-complexes and to understand the factors governing their pharmacology and toxicology.

T. Development of high-throughput methods and strategies to characterize the function of proteins and enzymes and/or define the functional interrelationships of proteins and enzymes.

U. Development of research tools to promote scientific collaboration in any of the above areas of research. For example, applications software for secure peer-to-peer networking to facilitate the exchange of scientific data and research materials or to construct a searchable distributed database.

Center for Bioinformatics and Computational Biology

A. Development and enhancement of databases for activities that fall within the mission of NIGMS.

B. Development of methods for data mining and providing integration and interoperability of different databases and varying modalities of data.

C. Development of tools to model complex biological systems that fall within the mission of NIGMS.

D. Design and development of software and hardware for improving the effectiveness of computational approaches in biomedical research.

Other Research Topic(s) Within the Mission of the Institute

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NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

The NHLBI plans, conducts and supports research, clinical trials and demonstration and education projects related to the causes, prevention, diagnosis and treatment of heart, blood vessel, lung, and blood diseases and sleep disorders. The NHLBI SBIR/STTR program fosters basic, applied, and clinical research on all product and service development related to the mission of the NHLBI. Research may be targeted to gender, race, or age subgroups.

For more specific information about areas of interest to the NHLBI, please visit our home page at http://www.nhlbi.nih.gov.

Research topics of interest include, but are not limited to research and development under the following specific initiatives as well as the topic areas listed under each of the NHLBI Divisions below:

Directed Stem Cell Differentiation for Cell Based Therapies for Heart, Lung, Blood, and Aging Diseases. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-124.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-125 (STTR)

Bioengineering Approaches to Energy Balance and Obesity. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-055.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-056.html (STTR)

Technologies for Monitoring and Performing Resuscitation. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-126.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-127 (STTR)

Development of Diagnostic Screening Test for Salt Sensitivity. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-033.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-034.html (STTR)

Phase II Competing Renewal Awards

The NHLBI will accept Phase II SBIR Competing Renewal grant applications from NHLBI-supported Phase II SBIR awardees that propose to perform research required to obtain Food and Drug Administration (FDA) acceptance or approval of the Phase II product in the form of an Investigational New Drug (IND), Investigational Device Exemption (IDE), 510K, Pre-market Approval (PMA) or a Humanitarian Device Exemption (HDE). This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Such products include, but are not limited to biological products, devices, drugs, vaccines, medical implants, etc. related to the mission of the NHLBI. The Competing Renewal application must be a renewal and logical extension of a previously completed NHLBI-supported Phase II (R44) SBIR grant. NHLBI grantees seeking SBIR Phase II Competing Renewal funding must submit an application no later than the first six receipt dates following expiration of the previous Phase II project budget period.

Budgets up to $1,000,000 total costs per year and time periods up to 3 years may be requested for this Phase II Competing Renewal opportunity. An applicant must provide evidence that their research plan and objectives follow FDA guidance for the development of a drug, biologic, or medical device. Examples of acceptable FDA guidance includes, but is not limited to, published guidelines and direct letters of communication from FDA personnel for an investigational new drug (IND) application, investigational device exemption (IDE), 510K, Pre-Market Approval (PMA), or Humanitarian Device Exemption (HDE). The applicant should also provide the status of their project in a timeline related to

Federal regulatory approval processes. An updated commercialization plan is also required.

Prospective applicants are strongly encouraged to contact NHLBI program staff prior to submission of an SBIR Phase II Competing Renewal application. Although it is not required, prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities.

- FDA-required pre-clinical studies beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants.
- Completion of pre-clinical and clinical studies required by the FDA for an Investigational New Drug (IND) application and New Drug Application (NDA).
- FDA-required pre-clinical and clinical safety and effectiveness studies of medical devices and tissue engineered products for an IDE or Pre-market Approval (PMA).
- FDA-required biocompatibility studies of surface materials of putative medical implants or other studies needed for 510k approval.
- FDA-required assessments of novel imaging systems.

Direct questions about scientific/research issues to:

Heart

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Heart and Vascular Diseases

The Division of Heart and Vascular Diseases plans and directs the NHLBI's research grant, contract, and training programs in heart and vascular diseases. These programs encompass institute- and investigator-initiated basic research, targeted research, specialized centers and clinical trials. The DHVD maintains surveillance over developments in its program areas and assesses the national need for research on the causes, prevention, diagnosis, and treatment of cardiovascular disease. The DHVD ensures that effective new techniques, treatments

and strategies resulting from medical research are transferred to the community through professional, patient, and public education programs in a timely manner.

The Division has three major programs: the Heart Research Program, the Vascular Biology Research Program, and the Clinical & Molecular Medicine Program, in addition to a Research Training and Special Programs Group.

Heart Research Program. Supports basic, applied, and clinical research in cardiac diseases, from embryonic life to adulthood.

Vascular Biology Research Program. Supports research in atherosclerosis, hypertension, cerebrovascular disease, cardiovascular complications of diabetes and obesity, basic vascular biology and gene and cell-based therapy for the prevention and/or treatment of vascular diseases.

Clinical & Molecular Medicine Program. Supports clinical, basic and engineering research on cardiovascular disease and health. Its scope includes genetic, genomic and proteomic research; cellular and molecular imaging; engineering theory and practice applied to biology and medicine including therapeutic cardiovascular devices and diagnostic instrumentation; nanotechnology; informatics and simulation; and cohort, case-control, and randomized clinical trials.

Research topics of interest to the Division of Heart and Vascular Diseases include but are not limited to the following:

A. Materials and Devices
   1. Angioscopes with increased flexibility and enhanced resolution.
   2. Medical implants (heart valves, vascular grafts, stents, pacemakers, defibrillators, etc.).
      a. Novel designs and materials.
      b. Failure prediction/analysis.
      c. Manufacturing.
      d. Monitoring.
      e. Preservation methods.
      f. Quality assurance and quality control.
      g. Reference biomaterials for evaluation of biocompatibility.
      h. Reliability.
      i. Biological response
   3. Circulatory support systems.
      a. Artificial heart.
      b. Ventricular assistance.
      c. Automatic control.
      d. New animal models for in vivo testing.
      e. Percutaneous and transcutaneous transmission of electrical energy.
      f. Implantable rechargeable batteries and alternate power sources.
   4. Biological, chemical, and mechanical sensors.
   5. Diagnostic instrumentation for the mouse and rat.

B. Methods
   1. Resuscitation-enabling technologies.
   2. Tissue engineering approaches and technologies that can be used to engineer functional tissue for repair or replacement of damaged or diseased tissue.
   3. Development of phenotypic screening methods in the mouse for heart, lung, and blood diseases and sleep disorders.
   4. Animal models for assessing genetic determinants of disease.
   5. Animal models of cardiovascular complications of diabetes mellitus.
   6. Nutrition and dietary interventions, products, software and databases.
   7. Lipid measurements and standardization in fresh human serum, without matrix effects.
   8. Systems biology approaches to study complex disease.
   9. Computational modeling approaches to study vessel wall biology.
   10. Mathematical and computer modeling of structure, function, and electrical activity of the normal and diseased heart.
   11. Computer modeling of hemodynamics in complex congenital heart disease.
   12. Metabolomics

13. Development of new and improved antisense agents and RNA interference (RNAi) technologies for cardiovascular disease therapies.
14. Gene and gene product relationship, structure, and function.
15. Gene discovery technologies.
16. Genetics of complex diseases--gene/gene and gene/environment interactions.
17. Gene assessment and diagnostic technologies.
18. Non-invasive methods of detecting cardiac rejection, particularly in infants and young children.
19. Non-toxic and selective molecular cages for delivering short-lived vasoactive agents to the vasculature.
20. Preservation methods for cardiovascular tissues or organs for use in transplantation and in research studies.
21. Technologies to assess energy balance and control weight.
22. Luminescent dyes to measure toxic metabolic intermediates in living cells in real time.
23. Novel use of information technology to enhance adherence to medical regimens or promote translational research.
24. Optimization of implantable defibrillator algorithms for arrhythmia prediction, efficient intervention, device fault detection or early failure detection.
25. Methods to increase success of cardiac xeno-transplants.
26. Methods to induce tolerance to cardiac allografts.
27. Non-invasive methods to diagnose cardiac allograft vasculopathy.
28 Animal models of cerebrovascular disease.
29. Novel techniques to study cerebrovascular disease.

C. Diagnostics and Treatment

1. Non-invasive diagnostic test for salt sensitivity.
2. Pharmacogenetics/Pharmacogenomics and personalized medicine.
3. Vascular and renal tubular fluid dynamics, non-invasive assessment.
4. Heart failure, early detection and treatment strategies.
5. Anti-hypertensive drugs from natural and synthetic sources.
6. Pro- and anti-angiogenic and vasculogenic genes, proteins and drugs.
7. Development of viral and non-viral vectors for gene therapy for cardiovascular diseases.
8. Vaccines for the prevention or treatment of atherosclerosis.

D. Imaging

1. Molecular imaging including imaging to detect gene expression.
2. New medical imaging systems, enhancements and applications.
3. Imaging characterizing vessel walls and lesions.
4. Neuro-imaging in hypertension.
5. Radiologic phantoms mimicking the human cardiovascular system.
6. Specific agents for high resolution imaging of the human lymphatic system.

Lung Diseases

The NHLBI Division of Lung Diseases (DLD) maintains surveillance over developments in pulmonary research and assesses the Nation's need for research on the causes, prevention, diagnosis, and treatment of pulmonary diseases. Also within the purview of the Division are: technology development, application of research findings, and research training and career development in pulmonary diseases. The DLD plans and directs the research and training programs which encompass basic research, applied research and development, clinical investigations, clinical trials, and demonstration and education research. Two programs comprise the Division of Lung Diseases: the Airway Biology and Disease Program, and the Lung Biology and Disease Program.

Airway Biology and Disease Program. Focuses on basic and clinical research, education and training related to chronic obstructive pulmonary diseases, asthma, cystic fibrosis, control of breathing,

bronchiolitis, respiratory neurobiology, sleep, and other adult airway diseases.

Lung Biology and Disease Program. Supports research, education, and training programs in lung cell and vascular biology; lung growth and development and pediatric lung disease; acute lung injury and critical care medicine; interstitial lung diseases, including pulmonary fibrosis and sarcoidosis; and AIDS and tuberculosis.

Research topics of interest to the Division of Lung Diseases include but are not limited to the following:

A. Diagnostic Tools.

1. Computer algorithms for reading and comparing chest radiographs and scans (computed tomography, radioisotopes, etc.) using digitized images.
2. Diagnose and treat respiratory abnormalities during sleep in infants, children, and adults.
3. Imaging techniques to monitor lung cell functions in vivo.
4. Non-invasive measurement of blood gases, hemodynamics and respiratory function in infants, in children, and in adults.
5. Non-invasive methodologies for measuring airways inflammation in asthma.
6. Non-invasive markers of lung disease activity.
7. Non-invasive methods to detect pulmonary thromboembolism, hypertension, and edema.
8. Probes to monitor peripheral tissue oxygenation in vivo.
9. Use of ambulatory monitoring techniques to diagnose and manage respiratory disorders of sleep.
10. Computerized tomography to quantify and monitor pulmonary disease processes.
11. Novel methods for bioassays.

B. Information and Health Education Tools.

1. Computer technologies to promote adoption and implementation of asthma clinical practice guidelines in medical practice.
2. Health education methodologies for patients, families, or communities to prevent or cope with lung diseases or to reduce their impact, especially among people with asthma who are minorities or living in poverty.
3. Improve smoking cessation programs.
4. Information systems to coordinate patient management and monitoring among patients and health care professionals.
5. Interventions to reduce passive smoking in infants and children.
6. Use of interactive and computer technology to teach self management to asthma and chronic obstructive lung disease patients.
7. Health education interventions on the recognition, management, or prevention of problem sleepiness and sleep disorders for the public, physicians, and other health care professionals.

C. Materials and Devices.

1. Blood substitutes to improve gas exchange.
2. Emergency, portable, and servo-controlled ventilatory support devices.
3. Improved aerosol delivery systems.
4. Improved devices for continuous oxygen administration, including airline travel.
5. Improved extracorporeal or implantable devices for blood gas exchange (artificial lung).
6. New approaches and technologies that can be used to engineer functional tissue, in vitro, for replacement or repair of damaged or diseased lung tissue, in vivo.
7. Personal exposure monitors for aeroallergens and other environmental pollutants.
8. Personal exposure monitors for measures of environmental exposures.
9. Thrombo-resistant materials for extracorporeal or implantable devices for blood gas exchange and for indwelling catheters.

D. Methods.

1. “Clean” animal models for Pneumocystis carinii infections.
2. Culture Pneumocystis carinii in vitro.

3. Determine viability and enumeration of infectious Pneumocystis carinii organisms.
4. Development and standardization of in vitro systems for the study of pulmonary epithelial (airway) cells and pulmonary endothelial (vascular) cells.
5. Identification of genes causing and modifying lung diseases.
6. Identify and detect lung cell specific differentiation markers.
7. Identify lung stem cell types.
8. Identify species and strain differences of Pneumocystis carinii.
9. Isolate, identify, and characterize cells found in pulmonary granulomas.
10. Methods to monitor levels of alertness or sleepiness continuously over extended periods of time.
11. Three-dimensional static, mathematical, cell culture models of airways and alveoli to define parameters determining aeropollutant absorption, deposition, and effects.
12. Develop technologies and tools for use in genomic or proteomic investigations of pulmonary diseases.

E. Treatments.

1. Delivery of specific drugs (e.g., antioxidants, artificial proteinase inhibitors, surfactant) and cell-based reagents to the lungs for treatment of pulmonary and non-pulmonary diseases.
2. Gene therapy for cystic fibrosis, alpha1antitrypsin deficiency, primary pulmonary hypertension, and other inborn errors of metabolism affecting the lungs.
3. Improved aerosol delivery systems.
4. Novel pharmacologic and gene therapy approaches for asthma, acute lung injury, idiopathic pulmonary fibrosis, and bronchopulmonary dysplasia.
5. Novel pharmacologic approaches for treatment of sleep apnea.
6. Pharmacological means of stimulating growth and repair of alveoli and reparative or restorative elastogenesis in lungs suffering emphysematous changes.

Blood Diseases and Resources

The NHLBI Division of Blood Diseases and Resources (DBDR) plans and directs research and research training and career development programs, emphasizing non-malignant blood diseases and disorders of thrombosis and hemostasis. The Division also has a major responsibility to improve the adequacy and safety of the nation's blood supply and to advance the study of stem cell biology and disease and novel cellular therapies. The Division has three major programs, the Blood Diseases Program, the Thrombosis and Hemostasis Program, and the Blood Resources Program.

Blood Diseases Program. Supports research and training for sickle cell disease, thalassemia, aplastic anemia and other red cell disorders from basic research on globin genes to clinical management.

Thrombosis and Hemostatis Program. Supports research and training in occlusive disorders involved in deep vein thrombosis, in cardiovascular diseases and stroke, and in bleeding disorders.

Blood Resources Program. Supports research and training in transfusion medicine, stem cell biology and disease, and clinical cellular medicine.

Research topics of interest to the Division of Blood Diseases and Resources include but are not limited to the following:

A. Animal models for blood diseases such as:

1. Anemias including: sickle cell disease, thalassemia, Fanconi anemia, Diamond Blackfan anemia, and other congenital anemias.
2. Bleeding disorders including: hemophilia, von Willebrand disease, and thrombocytopenia.
3. Platelet diseases.
4. Thrombosis and thrombolysis.
5. Hereditary hemorrhagic telangiectasia.
6. Paroxysmal nocturnal hemoglobinuria.
7. Hemochromatosis.
8. Myelodysplastic syndrome (MDS) and myeloproliferative disorders (MPD).
9. Hematologic malignancies.

B. Tools, reagents, and assays for hematologic research in mouse and other animals.

1. Nanotechnologies.
2. Non-invasive approaches to analytes.

C. Assays and technologies for:

1. Automated screening of therapeutic agents for blood diseases.
2. Anti-thrombotic drug monitoring and thrombosis screening.
3. Platelet functional tests.
4. von Willebrand disease.
5. Thrombotic Thrombocytopenia Purpura (TTP).
6. Multiplexed system for hemostatic factors, cytokines, and inflammatory agents.
7. Iron overload.
8. Blood-borne infectious agents transmitted by blood transfusion, including agents of transmissible spongiform encephalopathies and Creutzfeldt-Jakob Disease (CJD).
9. Diagnosis of inherited blood disorders.
10. Prolonging the in vivo lifetime of transfused red cells for therapeutic uses.
11. In vitro inactivation or removal of microorganisms from blood, blood components, and plasma derivatives.
12. Platelet storage methods that preserve biological efficacy.
13. Synthesizing, screening, and evaluating the safety and efficacy of therapeutic oxygen carriers.
14. Synthesizing or purifying plasma proteins for therapeutic use.
15. Measuring iron non-invasively.
16. Non-invasive measurement of blood cell counts or other blood components.

D. Drugs to Treat Hematologic Diseases and Cytopenic States

1. Anti-coagulants.
2. Anti-thrombotic agents.
3. Anti-sickling agents or other pharmacologic approaches to sickle cell disease.
4. Fetal hemoglobin enhancing agents.
5. Fibrinolytic and anti-fibrinolytic agents.
6. Iron chelators.
7. Replacement agents for hematologic factor deficiencies.

E. Cellular Therapies

1. Expansion of cell populations.
2. Production and standardization of immune-modulating cytokines or monoclonal antibodies.
3. Development of in vivo techniques to monitor survival, growth and development of engrafted cells.
4. Animal models for the demonstration of safety and efficacy of novel cellular therapies.

F. Gene therapy vectors and delivery systems for the treatment of hematologic genetic diseases.

G. Prothrombotic and hemorrhagic biomarkers and risk factors.

H. Computational models for blood diseases.

I. Bioinformatics to store and analyze genes, proteins, and biomarkers for hemostasis.

J. Equipment and procedures for the collection, separation, processing, preservation, storage, and distribution of blood and blood components.

K. Patient and physician health education programs to improve patient management and to prevent or reduce the impact of blood diseases.

L. Public Health Education.

1. Tutorials for community-based providers.
2. Community health education programs in sickle cell disease, suitable for use in faith-based organizations or other community settings.

M. Newborn Screening.

1. Genetic counseling programs for families of infants with hemoglobinopathies or trait.
2. Innovative data or surveillance systems to track follow-up and patient outcomes.

Epidemiology and Clinical Applications

The NHLBI Division of Epidemiology and Clinical Applications (DECA) plans and directs programs in epidemiologic studies, clinical trials of cardiovascular therapies, basic and applied behavioral research, demonstration and education research, and projects

for disease treatment and prevention as well as health promotion, including large scale clinical trials. The research supported by the Division provides multidisciplinary approaches to heart and blood vessel, lung, and blood diseases, and sleep disorders with a primary focus on cardiovascular disease.

DECA comprises two programs, the Clinical Applications and Prevention Program and the Epidemiology and Biometry Program, as well as the Office of Biostatistics Research.

Clinical Applications and Prevention Program. Supports research into prevention and treatment of heart and vascular, pulmonary, and blood diseases through activities such as efficacy and effectiveness clinical trials, health promotion/disease prevention trials, community intervention studies, nutrition research, and behavioral medicine research.

Epidemiology and Biometry Program. Supports and conducts epidemiological studies of heart and vascular, lung, and blood diseases in defined populations.

Research topics of interest to the Division of Epidemiology and Clinical Applications include but are not limited to the following:

A. Clinical research/intervention studies designed to improve cardiovascular disease outcomes.
   1. Approaches to facilitating adoption of evidence-based guidelines.
   2. Approaches to reducing clinical inertia in implementation of evidence-based guidelines for control of cardiovascular risk factors, including hypertension.
   3. Approaches to improving care of cardiovascular patients transitioning from hospital to ambulatory or home care.
   4. Approaches to improving prevention and treatment of ischemic heart disease (IHD), including prevention of recurring events and optimization of functional capacity in patients with IHD.

B. Clinical trial methodologies.

C. Community education and demonstration research studies.

D. Studies of cardiovascular disease information, education, prevention, and treatment systems for use in primary medical care and home care, including care by family caregivers.

E. Interactive databases.

F. Measures of patient adherence/compliance.

G. Assessment of polypharmacy, particularly for the elderly.

H. Methods for:
   1. Lifestyle intervention, including matching patients to lifestyle, intervention, or treatment.
   2. Health-care systems and outcomes research, including development of new quality measures for evidence-based cardiovascular health care.
   3. Quantitative measurement systems for behavioral and lifestyle variables, e.g., diet and physical activity.

I. Models of behavior modification and other approaches to behavior change.

J. Interventions in patients to promote healthy lifestyles, adherence to medications, and cardiac rehabilitation, including stress and exercise.

K. Treatment agents or strategies, including medications and devices.

L. Assay systems/techniques to measure patient responses to behavioral or medical interventions.

M. Materials, equipment and software for enhanced medical Imaging systems.

N. Methods for communication of research results.

O. Methods for collection, transmission, management and analysis of clinical data.

P. Nutrition, physical activity, obesity, stress reduction and smoking cessation interventions.

Q. Nutrition and physical activity measurement methods and devices.

R. Pharmaceutical development and toxicologic evaluation.

S. Population tracking mechanisms.

T. Psychosocial measurement instruments, especially in minority populations, including chronic social stress, depression, and discrimination.

U. Communication techniques for minority and low-income populations.

V. Prognostic assays.

W. Quality of life measurement and analytic methods.

X. Software for:

1. Clinical trials.
2. Epidemiology studies.
3. Literature abstracting.
4. Meta-analysis
5. Statistical analysis.
6. Shared clinical decision-making.
7. Monitoring and providing feedback to patients and providers in clinical care settings.
8. Analysis of context-dependent genetic effects.
9. Longitudinal data analysis
10. Microarray data analysis.
11. Automated systems for genotyping quality control and error checking.

Y. Screening, assessment, and tracking tools including biomarkers for hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.

Z. Survey questionnaires.

AA. Training techniques and modules.

BB. Interactive web-based programs for health promotion.

CC. Computerized systems to support evidence-based clinical practice in prevention and treatment of hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.

DD. Biomarkers for long term exposure to environmental factors including diet, physical activity, smoking, alcohol, and contaminants.

EE. Measures of gene expression in individuals.

FF. Cell immortalization, storage and distribution service.

GG. Standardized assays of glycosolated hemoglobin.

HH. Better measures of impaired glucose tolerance.

II. Simplified measures of sleep useful for population based studies.

JJ. Better measures of heart failure, including diastolic heart failure.

KK. Measures of small vessel disease.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

The scientific community now has available to it an extensive and large data set of genome resources and tools. The finished genomic sequences of many model organisms, the draft genomic sequences of human, mouse and rat, and the finished genomic sequences of a number of human chromosomes have been published. In addition, many other tools and technologies that allow these resources to be exploited are available, including microarray technologies and thousands of sequenced full-length cDNAs generated by the Mammalian Gene Collection. These resources can be used in creative and powerful ways to facilitate our understanding of human biology.

With the completion of many of the original goals of the Human Genome Program, the NHGRI unveiled its vision for the future of genomics in April 2003 (http://www.nhgri.nih.gov/11006873). The vision has three major themes- (1) genomics to biology; (2) genomics to health; and (3) genomics to society. There are also six cross-cutting areas which support the vision: technology development, computational biology, resources, training, education, and ethical, legal and social issues.

The success of the Human Genome Project has been due in large part to the development of improved technologies, strategies and methods that can be applied on a genome-wide scale in a cost-effective manner. As the vision of genomics expands, the development of new and improved technologies will be even more important in helping to accomplish the NHGRI's new research goals. Therefore, the NHGRI solicits SBIR/STTR grant applications in the areas listed below. Innovative and new approaches in other areas not listed in the major topics below, but that are relevant to genomics, will also be seriously considered.

DNA Sequencing

The ultimate goal of the DNA sequencing technology program is to develop technologies that can generate accurate DNA sequence from whole genomes in a short time and at a very low cost (e.g., $1000 for a mammalian-sized genome). To achieve that, more near-term goals include the development of innovative, cost-effective technologies and strategies to (1) reduce the cost, increase the throughput, or improve the accuracy of large-scale DNA sequencing of complex genomes; (2) obtain DNA sequence in the gaps that are left by current sequencing methods or improve the efficiency of sequencing in genomic regions that have proved difficult to sequence due to limitations in available cloning and sequencing technology; (3) determine sequence in regions of difference between closely-related organisms; (4) determine the sequence of any particular region of a genome and its syntenic regions from genomes of several other species; (5) rapidly and cost-effectively determine the sequence of one or more large (megabase) genomic regions from many individuals of a single species (e.g., human) for mutation detection; and (6) rapidly and cost-effectively resequence entire genomes to detect polymorphism. Instrumentation and methods development from feasibility through prototype development and introduction into production are supported. Any applicable technology approach is welcomed; micro- and nanotechnology approaches are particularly encouraged.

Human Genome Sequence Variation

Development of new or improved methods and analytic tools for: (1) the large-scale identification, scoring, and interpretation of DNA sequence variants; (2) the identification of haplotypes and generation of haplotype maps; and (3) facilitation of studies relating genetic variation to association with disease, to gene mapping, and to an understanding of chromosomal and population processes.

Comparative Genomics

Improvement in the technology for generating clone libraries useful for genomic analysis with DNA inserts that are stable, free of artifacts, and faithfully representative of genomic DNA from complex organisms. Also of high priority is the development of technology to generate physical maps efficiently and rapidly.

Functional Genomics

Development of new or improved technologies for large-scale or genome-wide approaches relating to: (1) gene discovery, full-length cDNA synthesis, or gene expression analysis; (2) improved or new technologies that are more efficient for isolating cDNAs for mRNAs that are rare or long (>4kb), or both; (3) analysis of the products of gene expression (e.g., proteins, metabolites), their identification in biological samples, their modifications, their interactions; (4) functional analyses of non-coding sequences; (5) generation and detection of mutations; and (6) innovative instrumentation used in screening for chemical modifiers of function, i.e., chemical genomics. Micro- and nanotechnology approaches are particularly encouraged.

Bioinformatics and Computational Biology

Development of new or improved tools for: (1) obtaining, representing, analyzing and archiving data; (2) assembling sequence data; (3) extracting information from comparative genomic sequences; (4) improving databases, in the areas of DNA sequence, gene mapping, complex trait analysis, genetic variation and homology, and functional genomics; (5) editing and implementing controlled vocabularies for genomic and phenotypic information; and (6) integrating genomic and genetic data for the purpose of identifying and modeling genetic pathways and networks.

Bioinformatics Education

Development of new educational curricula and tools to facilitate the teaching of (1) bioinformatics to high school and college students and (2) genomics, genetics, and bioinformatics approaches to understanding human biology and disease to physicians.

Ethical, Legal and Social Implications (ELSI) of Genomics and Genetics Research

Examination of issues surrounding the commercialization of genetic technologies, including issues relating to patenting, licensing, and other intellectual property concerns.

Other Research Topic(s) Within the Mission of the Institute

Individuals interested in any of the above listed areas are encouraged to contact the NHGRI staff listed below. For more specific information about areas of interest to the NHGRI, please visit our home page at http://www.genome.gov/Grants/.

For additional information on research topics, contact:

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For administrative and business management questions, contact:

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NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, translational research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro-AIDS research). Ultimately, this research will lead to greater understanding, better treatment and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through

scientific communications and public education, and in its more effective implementation in practice and service delivery systems. There is a general need to develop reliable and inexpensive products, that can serve these needs.

For additional information about areas of interest to the NIMH, please visit our home page at http://www.nimh.nih.gov.

Phase II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-079.html.)

The NIMH will accept Phase II SBIR Competing Renewal grant applications to continue the process of developing technologies that ultimately require federal regulatory approval. Such technologies include, but are not limited to, pharmacologic agents and drugs, biological products, devices, vaccines, etc., related to the mission of the NIMH. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Budgets up to $800,000 total costs per year and time periods up to 3 years may be requested for this Phase II Competing Renewal opportunity.

Please contact your Program Director or Dr. Margaret Grabb (contact information provided below) before beginning the process of putting an application together. In addition, prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIMH SBIR Phase II awards will be eligible for a Competing Renewal grant.

The following examples would make appropriate topics for proposed NIMH SBIR Phase II Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities:

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants. Some in vivo or in vitro studies would be expected to have been carried out in Phase I or the initial Phase II grant.
- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.
- Studies in normal healthy volunteers to determine a drug's safety profile, metabolism, etc.
- Clinical studies in patient/disease population to assess the drug's effectiveness.
- Assessment of devices with regard to performance standards related to the FDA approval process.
- Safety and effectiveness studies of novel medical devices.
- Evaluation of novel imaging approaches for diagnostic purposes.
- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Direct your questions about scientific/research issues to:

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Division of Neuroscience and Basic Behavioral Science

Through research in neuroscience and basic behavioral science we can gain an understanding of the fundamental mechanisms underlying thought, emotion, and behavior and an understanding of what goes wrong in the brain in mental illness. Research sponsored by the Division of Neuroscience and Basic Behavioral Science covers a broad range of neuroscience topics: from both experimental and theoretical approaches, from molecules to whole brains to populations of individuals, from single cell organisms to humans, from across the entire lifespan, and from states of health and disease. This division also supports research on the basic behavioral, psychological, and social processes that underlie normal behavioral functioning. The topics listed below reflect the NIMH interest in technologies related to this broad range, but should not be considered a complete list. Prospective applicants are strongly encouraged to contact Dr. Margaret Grabb (listed below) with questions about the relevance of their interests to the mission of this division.

A. ***Cutting-Edge Technologies for Neuroscience Research.*** Most of the research topics listed after this one are posed from the Division's neuroscience and basic behavioral science mission-oriented perspective, however, the technologies that might be developed to address those mission goals might be quite fundamental. Prospective applicants familiar with such technologies, but not familiar with the mission-related use of these technologies, are strongly encouraged to contact Dr. Margaret Grabb (listed below) for assistance in bridging this gap between their technical knowledge and knowledge of the neuroscience-related mission of NIMH. Technologies and approaches that might be used in products relevant to this mission include, but are not limited to:

1. *Caged Molecules*. These chemical entities could be activated, or could release an active agent, when specified bonds are broken by chemical, biochemical, photic, or other means. Among other uses, such molecules could be used to indicate biochemical or physiological processes or to deliver pharmacologic substances to highly localized brain regions.
2. *Genetically Engineered Proteins*. Such proteins could be put to any number of uses, including to express a fluorophore or chromophore at the occurrence of specific biochemical processes to report the time and location of such processes in brain tissue.
3. *Inducible Gene Expression*. Methods to turn on or off expression of particular genes in transgenic animals on the basis of time in the lifespan, location in the brain, or other factors. Such a capability would significantly advance basic brain research, and would have important implications for treatment and therapy of mental illness.
4. *Combinatorial Approaches*. These are high-through-put approaches that can be used to screen and synthesize molecules that affect brain cells.
5. *Biocompatible Biomaterials*. Such research and development relates to the chronic use of electrodes and other probes used in brain research, as well as implanted drug delivery devices.
6. *Nanotechnologies*. This emerging area of technology presents a wide range of opportunities for brain research, from the fabrication of probes to monitor brain physiology to novel means of delivering drugs and other substances.
7. *Informatics Tools*. Such technologies allow brain scientists, clinicians and theorists to make better sense and use of their data. These tools and approaches include those to acquire, store, visualize, analyze, integrate, synthesize and share data, including those for electronic collaboration.
8. *Simulation Technologies*. Computer-based simulations of parts of neurons, neurons, circuits or even organisms to observe the manner in which these components interact. For example, simulations of individual organisms with constellations of particular traits that vary across individuals would allow analysis of their interactions and their impact on the population as a whole.
9. *Mathematical, Statistical and Computer Algorithms*. Such algorithms could be used to analyze large and/or complex data sets. Examples of these data sets include those derived from multiple, single-unit recording studies and functional imaging studies. Among other applications, these could be used to segment images (obtained from

electron or light microscopes, or from volumetric imaging instruments such as confocal microscopes and magnetic resonance imagers), filter noise, visualize data or search vast data sets for specified patterns or data (e.g., use of pattern recognition algorithms to search time series data sets obtained from electrophysiological recording of neural activity, or video data obtained from behavioral analysis of genetically altered animals). Improved techniques for path analysis when examining functional imaging datasets would also be of interest.

10. *Telemetry*. Transferring data from one point to another is important for neuroscientists monitoring the physiological signals from the brain. Telemetry, even over relatively short distances (from a few millimeters to a few meters), could, for example, provide a means to obtain data from awake, behaving animals without interfering with the behavior of interest.

11. *Biosensors*. Neurons communicate with each other through thousands of different chemical substances; internally, molecular pathways direct the function of the neuron. Sensors of high specificity and sensitivity for such substances would provide neuroscientists with important new ways to study the brain.

B. ***Instrumentation for Basic Neuroscience Research.*** Modern equipment that uses the most recent technological advances is needed in neuroscience research so that neural substrates of mental illness can be identified and localized. The NIMH is interested in supporting research and development of new or improved approaches relevant to, but not limited to, the following:

1. *Neurophysiology*. Microelectrodes, smart nanoscaffolds, macroelectrodes, biocompatible coatings, interfaces to electronics, software for data analysis, visualization, etc.

2. *Cell Sorting*. Based on cell size, type, function, etc.

3. *In Vivo Electrochemical Voltammetry*. More sensitive and selective electrodes, software for data analysis, etc.

4. *High Performance Liquid Chromatography*. Improved reliability, specificity, sensitivity, etc.

5. *Technology to support Multiple Unit Recording Electrode Arrays*. Both recording techniques and analysis techniques.

6. *Physiological and Behavioral Monitoring*. Temperature, activity, sleep duration, neuronal activity, EEG activity, EKG, pulse rate, recording, capture and analysis of multiple single unit activity from microelectrodes.

7. *Associated Software*.

C. ***Macroscopic Neuroimaging.*** Modern technologies allow for the observation of the structure and function of the intact brain. This capability has the potential to greatly advance understanding of the brain in both health and disease, and across the lifespan. NIMH is interested in advancing this area of technology through enhancing current tools and approaches, as well as developing entirely new ways to image the brain. All modalities are of interest, including, but not limited to: magnetic resonance imaging (MRI) or spectroscopy, positron emission tomography (PET), optical imaging or spectroscopy, single photon emission computed tomography, magnetoencephalography (MEG), diffusion tensor imaging (DTI), etc. While not an imaging technique itself, transcranial magnetic stimulation (TMS) is an associated, important technology. Due to its greatly increased use in recent years, technologies specifically focused on improving the utility of fMRI techniques are of particular interest.

1. Innovative agents and/or technologies to visualize brain connectivity in situ with minimal invasion.

2. Improvement in the techniques, the design and construction of devices for non-invasive imaging for any modality, for example, improving spatial resolution, quantitative accuracy, signal-to-noise ratio, and electronics.

3. Development and enhancement of non-invasive imaging techniques for evaluating alterations in brain physiology produced by drugs. These would include techniques for monitoring changes in regional blood flow; concentrations of tissue metabolites; and the distribution and activity of receptors.

4. Synthesis, or isolation from natural products, of highly selective receptor ligands or indicators of neurochemical processes, which would be labeled for imaging by one or more particular modality.
5. New approaches in radiochemistry that will permit more exact identification of the chemical changes associated with behavioral states (e.g., sleep or arousal) or mental illness as observed with any particular neuroimaging modality.
6. Synthesis of molecules containing stable, rarely occurring isotopes designed to be detected by non-invasive imaging techniques (e.g., fluorine-containing molecules, carbon-13 labeled substrates).
7. Methods and associated products for quantitation of imaging data including new statistical approaches for evaluating the data.
8. Methods to integrate routines for greater and more precise computer enhancement of the images, and for combining or overlaying images obtained from multiple modalities.
9. Software needed for the precise quantitation of data obtained from these imaging techniques with emphasis on the reliable definition of discrete, anatomically distinct areas within the brain.
10. Novel agents or other tools to increase the ability to correlate features of MRI images with histological features (e.g., cytoarchitecture or chemoarchitecture) both identified and those yet to be identified.
11. Generation of physiologic measurements from images of regional radioactivity generated during PET, especially for the study of brain neurotransmitter/ neuroreceptor systems.
12. Novel approaches to visualizing data obtained in neuroimaging, such as the computational “unfolding” of three-dimensional images of cerebral cortex.
13. Improved methods for pediatric brain imaging. These would include: software and database products, equipment for creating a “child-friendly” environment and for the behavioral training of children and impaired subjects for cooperation and motion reduction during neuroimaging procedures.
14. Combining of different imaging technologies (e.g., ERPs and fMRI; MEG and fMRI; MEG and EEG, etc).
15. Development of equipment, software and other tools for recording and quantifying eye movements, motion, and autonomic reactivity during scanning, applicable to all ages (including young children) particularly in the MRI environment.
16. Methods for relating changes in brain morphology and metabolism associated with age, particularly infancy through adolescence, to changes in hemodynamic responses to neural activity and fMRI signals.
17. Improvements in TMS techniques that will allow for greater specificity in the sites of stimulation and greater control over the effects of the stimulation.

D. ***Microscopic Neuroimaging.*** The morphology of individual neurons and the distribution of subcellular components within them, are key to understanding the manner in which these cells function. Advances in the development of agents indicating neuronal structure and function that can be visualized microscopically are important to the NIMH's interest in brain research. This includes enhancements of current agents and ligands to be imaged (agents indicating specific biochemical processes or structures, etc.); development of novel agents and ligands; software to assist interaction with the data; and other related technologies and methods. Examples would include, but not be limited to:

1. Software and hardware for analyzing image data obtained by microscopes, including tools to automatically or semi-automatically. Identify particular profiles (e.g., labeled cell bodies), segment images, reconstruct images into three dimensional representations, perform unbiased counting and measuring, etc.
2. Synthesis and testing of novel or improved probes for microimaging the nervous system.

E. ***Molecular and Cellular Neurobiology and Neurochemistry.*** Manipulating and studying basic molecular, cellular and chemical

processes has led to insight to understanding brain function, and has provided the foundation on which pharmacological interventions have been developed for the treatment of mental illness. NIMH is interested in supporting a wide range of new techniques and tools related to this area. These include, but are not limited to:

1. New low-cost techniques for hybridoma production of monoclonal antibodies specific for "neural antigens" (e.g., neurotransmitters, small peptides, neurotransmitter receptors).
2. Innovative methods for establishing a "monoclonal bank" (frozen cells) for each of the cell lines as a permanent, widely available, reliable, and low cost source of monoclonal antibodies for research on the nervous system.
3. Labeled antibodies or other agents that will readily identify receptors for which there are no ligands (orphan receptors) and which have low densities in the brain.
4. Automated methods for quantitating the low levels of bound ligands for quantitating receptors that are sparsely scattered in the brain.
5. New cell lines that express each of the known neurotransmitter receptors so that each cell line will be homogeneous for one receptor.
6. New cell lines that express each of the above receptors linked to some metabolic function and/or second messenger so that the functional consequences of receptor occupancy can be detected.
7. High volume, inexpensive assay methods for measuring both receptor occupancy and cellular response for each of the receptor types.
8. Develop cell culture models for neurons, including methods of purifying homogeneous populations of non-transformed cells by, for example, developing markers to identify neuronal cell types for use in characterizing cell-type-specific signaling pathways which may be useful in tracking the effects of various drugs.
9. Develop techniques for either activating or deactivating specific ion channels, receptors and signal transduction pathways.
10. Develop dynamic biochemical and imaging assays that allow measurement of variables now obtained only through electrophysiological techniques.
11. New approaches to study the multiple functions of particular proteins.
12. Tools to study post-translational changes in proteins in specified tissue compartments.
13. Technologies to study functional entities within cells (e.g., green fluorescent protein approaches).
14. Tools and approaches to study coordinate changes in genes and their functional relationship to phenotypes, including phenotypes associated with specific brain disorders.
15. New ways to assess quantitatively transcription of genes in real time in a manner that is minimally injurious to cells (e.g., non-permeabilizing approaches).
16. Novel tools and approaches to study protein-protein interactions, especially those with phosphoproteins. Further develop methods and reagents for studying the structures of membrane proteins at atomic resolution. Membrane protein systems that are of particular interest to NIMH include proteins involved in normal function and pathology of cells (neurons and glia) in the central and peripheral nervous system.
17. Develop novel techniques for isolating and identifying the structure of brain-derived membrane proteins.

F. ***Genetic and Transgenic Technology.*** Advances in genetic and transgenic technologies offer many opportunities to probe fundamental questions about the brain, behavior and pathology. NIMH is broadly interested in these areas; some examples of topics relevant to the mission of this Institute include, but are not limited to:

1. Methods to perform site-directed mutagenesis in cell lines for the study of membrane proteins such as ion channels and neurotransmitter receptors.
2. Development of gene "knockout" or "knockin" animals using such approaches

as homologous recombination targeting genes important in neurotransmission, development, and tropic interactions as well as in generating behavioral models of disease.

3. New methods to delete or alter targeted genes in the preparation of transgenic animals including methods that increase or decrease gene expression.
4. Development of new techniques and apparatus for delivery of antisense oligonucleotides into cells and specific tissue such as the brain.
5. Develop standardized behavioral tests to assess the gene knockouts and/or gene "knockins" affecting neurotransmission.
6. New approaches for cell-specific, tissue-specific, age-specific, transient gene activation and/or inactivation.
7. Innovative technologies to study gene function and expression.
8. Development of embryonic stem (ES) cell lines from rodent strains (rats and mice) of relevance to behavioral research.
9. Development of technologies and approaches to facilitate the collection and distribution of ES cell lines containing mutations of potential relevance to behavioral research.
10. Develop methods for long-term storage of transgenic germ cell lines.
11. Develop technologies and approaches to aid in the renewal of founder colonies of transgenic mice from repositories of transgenic germ cell lines.
12. Develop databases on neurobiological transgenic animals produced to date, including information such as the origin of the transgenic animal, key features of the biological and behavioral mutant, availability and location of germ cell lines, and existence of breeding colonies.
13. Develop gene transfer technologies such as viral vectors to produce long-term, stable gene expression in the brain.

G. ***Neuroimmunology.*** Research on the interplay between the brain, neuroendocrine system, and, immune system has revealed important links between these major homeostatic system components. Examples of NIMH-relevant topics in this area include, but are not limited to:

1. Development of new tools to explore the special properties of the blood-brain barrier responsible for the selective delivery or retention of cytokines, immune cells, and drugs affecting immune activity in the brain.
2. Development of assays for identifying potential autoimmune components of psychiatric disorders (other than the usual screening for "markers").
3. Identification of critical molecules, processes, and pathways mediating signals from the peripheral immune system to the brain.
4. Development of novel cytokine ligands and antagonists.

H. ***Pharmacology.*** Pharmacological intervention represents a major force in the treatment of mental illness, and NIMH is interested in supporting research and development in this area. Relevant topics include, but are not limited to:

1. New chemical entities with high, selective affinities for each of the receptors in the brain.
2. Methods to evaluate old and new chemical entities (including complex mixtures of crude extracts from natural products) for possible therapeutic usefulness using "in vitro" and "in vivo" assays and model systems.
3. Methods for extraction, fractionalization, and isolation of active compounds from natural products. Water-soluble compounds are of particular interest due to the difficulty of the procedures.
4. Computer algorithms that model receptors to evaluate theoretical permutations of known molecules to find the molecule with the maximum probability of having the highest affinity for a specific receptor as well as those that have the potential for the most desirable "on" and "off" rates.
5. Computer models of the blood brain barrier and evaluate potential and actual drug molecules for their ability to cross or penetrate this barrier.

6. Strategies for evaluating pharmacological agents (e.g., animal behavioral testing, computer simulation) on cognitive function.
7. Behavioral "models" similar in animals and humans; behavioral pharmacological effects that may serve as "surrogate" markers in humans.
8. Development of novel drug delivery systems.
9. Tools for Drug Development including neuroimaging (e.g., radiolabeled compounds) and development of animal models.
10. Pharmacological profiling (in vitro and in vivo) for potential therapeutic drugs.
11. Methods for evaluation of long-term effects of psychotropic drug administration in animal models or human subjects. If clinical populations are being tested, the technology would be appropriate for either the Division of Pediatric Translational Research (DPTR) or the Division of Adult Translation Research (DATR) at NIMH.
12. Improving existing, and developing new, vectors for delivery of genes to the brain.
13. Development of novel therapeutic approaches based on drug-induced changes in gene promoter activity.
14. Development of novel high throughput screening (HTS) assays for drug development. Examples include, but are not limited to, in vitro functional assays, toxicology screens, blood-brain barrier permeability assays, and behavioral assays.
15. Development of novel molecular targets for drug development to treat mental illnesses.

I. ***Tract Tracing Methods and Tools.*** Little is known about the details of the connectivity of the human nervous system, because the best tract tracing techniques are invasive and require the deposit of substances in vivo. Methods that would be applicable to post-mortem tissue would allow significant progress in connectional studies of human tissue, as well as non-human tissue, particularly with regard to the development of connections and the connections of structures not easily accessed in vivo.

J. ***Basic Behavioral Science.*** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer-based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.

1. *Methodological Research and Development*. There is a need to devise new ways of data collection, analysis, management and dissemination. The goal is to encourage research that will improve the quality and scientific power of data collected in the behavioral and social sciences, relevant to the mission of NIMH. Research that addresses methodology and measurement issues in diverse populations, issues in studying sensitive behaviors, issues of ethics in research, issues related to confidential data and the protection of research subjects, and issues in developing multidisciplinary, multimethod, and multilevel approaches to behavioral and social science research is particularly encouraged.
   a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
   b. Computer software to ease analysis of behavior monitored by video or telemetry systems.
   c. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of a person's behavioral or physiological responses to group interactions.
   d. Causal modeling methodology as applied to correlational longitudinal data sets.
   e. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.
   f. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection

for experiments on perception and cognition.

g. There is a need for the development of hardware for time-stamped diary collecting instruments for use in actigraph studies of circadian rhythms in adults, children, and adolescents. Diaries are critical for the evaluation of activity data, and time-stamped diary collecting instruments can ensure investigators of receiving reliable information.

h. Web-based software tools for designing, updating, sharing, linking, and searching databases containing detailed information about the methodology and results of behavioral science studies.

2. Diagnosis and assessment of emotional and psychological states such as automated methods to detect specific emotional states using behavioral and autonomic indicators.

a. *Physiological Monitoring*. Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:

i. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.

ii. New techniques for electrophysiological images from the level of the single cell and surface EEG recording on the scalp.

iii. Small, portable automated systems to monitor eye function (e.g., pupil size, accommodation) and eye movements.

iv. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real-time.

b. *Measurements of Infant Development Using Physiological and Behavioral Measures*.

i. Psychophysiological measures to evaluate infants during the first six months of life.

ii. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).

iii. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.

iv. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.

c. *Behavior Monitoring and Analysis*.

K. ***Educational Tools.*** Neuroscience and basic behavioral science are compelling areas of science that not only touch upon a diverse array of disciplines, but also provide insights to the essence of what it is to be human. Products aimed at teaching the substance of these fields to students of all ages would be useful in disseminating this information and these insights. Examples include, but are not limited to: software and other interactive media used to convey fundamental concepts about the brain to children; computer simulations of neuroscience experiments; updateable media that presents state-of-the-art information on particular topics for use by experts; website or other online, interactive electronic vehicle to allow for sharing of information about the brain and its functions, including technologies for holding interactive research conferences related to basic behavioral sciences, basic neuroscience, or clinical neuroscience.

L. ***Neuroinformatics.*** Data generated by brain research are diverse, vast, and complex. The diversity of data is due to the fact that neuroscience data are obtained from: theoretical, experimental and clinical approaches; from levels of biological organization that span molecules to populations

of individuals and from single-cell organisms to humans; and from states of health, disease, and models of disease. The quantity of data in brain research is the result of tens of thousands of neuroscience laboratories working around the world. The complexity of data reflects the high level of interconnectedness of the data, and their high dimensionality. Neuroinformatics is a new area of science that draws upon neuroscience, information science, computer science, statistics, applied mathematics, and a variety of engineering fields to develop tools that will let neuroscientists make better sense and use of their data. These tools include software and hardware for digital data acquisition, visualization, analysis, integration, and sharing (e.g., through tools for electronic scientific collaboration). Such tools can address data of any type or from any area of neuroscience; examples include, but are not limited to:

1. Databases, querying approaches, and information retrieval tools for neuroscience and neuroscience-related data.
2. Tools for neuroscience data visualization (and other forms of presentation) and manipulation (probabilistic atlases of brain structure or function, new statistical approaches for analyzing data, etc.).
3. Software for integration and synthesis of neuroscience data (computational models of neurons to integrate data about structure and function, environments to merge data from multiple imaging modalities, etc.).
4. Tools for electronic collaboration to allow neuroscientists to interact with colleagues, data, and instruments at a distance (this could include novel types of “groupware”, etc.).
5. Tools that bridge existing neuroscience and biology information tools and resources, such as databases and informatics tools associated with genome mapping efforts.

M. In addition, we have special interests further detailed in the following Program Announcements (PAs):

1. Innovations in Biomedical Computational Science and Technology: SBIR/STTR Initiative http://grants.nih.gov/grants/guide/pa-files/PAR-06-088.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PAR-06-089 (STTR).
2. Development of PET and SPECT ligands for brain imaging http://grants.nih.gov/grants/guide/pa-files/PA-06-017.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-018.html (STTR).
3. Pharmacologic Agents and Drugs for Mental Disorders http://grants.nih.gov/grants/guide/pa-files/PA-06-027.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-028.html (STTR).
4. Competing Renewal Awards of SBIR Phase II Grants for Pharmacologic Agents and Drugs for Mental Disorders http://grants.nih.gov/grants/guide/pa-files/PA-06-079.html.
5. Probes for Microimaging the Nervous System http://grants.nih.gov/grants/guide/pa-files/PA-06-021.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-022.html (STTR).
6. Knowledge Integration across Distributed Heterogeneous Data Sources http://grants.nih.gov/grants/guide/pa-files/PA-06-011.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-010.html (STTR).
7. High Throughput Tools for Brain and Behavior http://grants.nih.gov/grants/guide/pa-files/PA-06-023.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-024.html (STTR).
8. Bioengineering Nanotechnology Initiative http://grants.nih.gov/grants/guide/pa-files/PA-06-008.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-009.html (STTR).

For further information on basic neuroscience or basic behavioral science research topics, contact:

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The Division of Pediatric Translational Research and Treatment Development

The Division of Pediatric Translational Research and Treatment Development directs, plans, and supports programs of research and research training leading to the prevention and cure of childhood psychopathology. This long-term goal will be accomplished through an integrated program of research across behavioral/psychological processes, brain development, environment and genetics. The topics listed below reflect the NIMH interest in technologies related to this research area, but should not be considered a complete list. Prospective applicants are strongly encouraged to contact Dr. Margaret Grabb (listed below) with questions about the relevance of their interests to the mission of this division.

A. ***Technologies for Clinical Pediatric Research.*** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior, as well as normal and abnormal physiological and biochemical functions, in human development. Computer-based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community. Examples include:

1. *Measurements of Alterations in Pediatric Development in Patients with Mental Health Disorders Using Physiological and Behavioral Measures*. Research studies indicate that some mental health disorders, such as autism, may begin to develop as early as infancy. Therefore non invasive modern equipment that use the most recent technological advances are needed to isolate specific physiological and behavioral changes during development, to identify potential diagnostic markers of mental health disorders. A priority for this program is to support research and development of hardware and software tools to measure pediatric development. Examples of technologies needed include:

   a. Psychophysiological measures to evaluate infants, children or adolescents.

   b. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).

   c. Telemetry capability for non-invasive devices so that children can be monitored for prolonged periods without interfering with their behavior.

   d. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.

2. *Pediatric Assessment Tools:* Diagnosis of mental health disorders in children and adolescents is vital to providing early interventions to treat the disorder. In addition, a better understanding of the concept of functioning in psychopathology, and its appropriate measurement, is needed in pediatric populations. In the future, diagnostic tools may even help detect the initial onset of illness in children at risk, before symptoms occur. A priority for this program is to develop novel diagnostic tools to detect mental health disorders in children and adolescents. Biochemical, genetic, physiological and psychological tool development is welcomed.

   a. Technologies to assess CNS effects of psychosocial or pharmacological interventions.

   b. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

   c. Computerized methodologies for assessing various mental disorders suitable for use in primary care settings.

   d. Measures that quickly, and reliably assess mental disorders that are co-morbid with other mental disorders or with substance abuse disorders.

   e. New technologies to assess and validate occurrence of and injuries resulting from child abuse and neglect.

   f. Behavioral and laboratory measures to define and assess specific impairment-

related components of psychiatric disorders, e.g., cognitive dysfunctions in schizophrenia.

g. Biologically based technologies that will aid medical doctors in determining how a particular individual may respond to a particular medication, i.e. "individualized medicine". For example, genomic and phenotypic information combined could be used in determining whether a drug will be an effective treatment for an individual. Likewise, genomic and phenotypic information may help to identify which patients are at risk for drug-induced side effects.

h. Development of valid and reliable measures that operationalize functioning within and across developmental periods, and that can be used in a variety of service settings. Such measures can lead to more accurate diagnoses, a better understanding of the impact of psychiatric disorders, and better tracking of treatment effectiveness.

3. *Behavior Monitoring and Analysis of Pediatric Mental Health Disorders*.

a. Improve or create new video devices to monitor human behavior and ease analysis of behavior.

b. Computer software to ease analysis of behavior monitored by video or telemetry systems.

c. Automated methods to detect specific emotional states using behavioral and autonomic indicators: This Division is specifically interested in technologies that can identify children with heightened or dampened emotional states that could be associated with particular mental health disorders. If the technology will primarily be used to investigate basic mechanisms of behavior, the Division of Neuroscience and Basic Behavioral Science at NIMH would be the most appropriate division to contact.

4. *Methodological Research and Development*. There is a need to devise new ways of data collection, analysis, management and dissemination. Examples include:

a. Instrumentation and equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.

b. Innovative, computer-based methods to monitor preventive and treatment intervention efforts and correlate them with outcome measures are needed. Results should be accessible to other interested parties without compromising the privacy of the individual.

c. Development of innovative software for addressing the integration of distributed cross-disciplinary data sources into coherent knowledge bases. The data should focus on pediatric mental health disorders.

d. Computer-based intervention development for parents or for school settings.

e. Video-based instruction for prevention of mental disorders, to be used by parents or in school settings.

f. Development of databases containing detailed genetic and behavioral information on pediatric populations and their families, as resources for the field in investigations of gene x environment interactions.

B. ***Child and Adolescent Treatment and Preventive Intervention Research.*** An estimated one in ten children and adolescents in the United States suffers from mental illness severe enough to cause some level of impairment. Yet, it remains unclear what treatments are the best and safest for these developing age groups. A priority for this program is to support research and development of novel psychopharmacological or psychosocial approaches for the treatment and prevention of mental illness in childhood and adolescence, in subjects aged 18 and below.

The goal of this research is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, and the range of outcomes measured. Disorders

studied include all mental and behavioral disorders. Interventions studied include pharmacologic approaches (individual and combination medications), somatic approaches, behavioral and psychotherapeutic approaches. Research is supported on individual and combined approaches. Research that translates findings on basic physiological or behavioral processes into novel preventive or treatment interventions is especially encouraged. Effectiveness studies that focus on interventions of known efficacy are assigned to the Division of Services and Intervention Research.

Human subjects include child and adolescent age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders and behavioral problems (e.g., anxiety and depression) and substance abuse (e.g., depression and alcohol abuse). Examples of the research support include: trials to establish the short- and long-term efficacy of interventions and off-label or innovative applications of established interventions.

1. *Pharmacologic Treatment Intervention.* Areas include clinical psychopharmacology, new/innovative applications for established treatments (off-label use), and somatic treatments. Also included are studies to determine the safety of interventions that have not been shown to be efficacious. It is expected that compounds have received IND approval and will be tested clinically in this program.
2. *Combined Intervention*. Areas include all research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention).
3. *Psychosocial Intervention*. Areas include development and application of new psychotherapeutic, behavioral, and psychosocial treatments.
4. *Preventive Intervention Program*. Areas include preventive intervention studies in which efficacy has not been demonstrated, including those designed to reduce the risk of onset or delay onset of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence) or side effects (prevention/ minimization of tardive dyskinesia, etc.). Prevention studies in schools and community settings are also encouraged.

C. ***Science Education in Mental Disorders.*** There is a critical need for improvement in science education, particularly in areas specifically related to brain, behavior and mental illness. Examples include:

1. Research on the best ways to present neuroscience and behavioral science information, in the context of mental health disorders, to particular groups of students (e.g., kindergarten through sixth grade).
2. Computer-based systems to teach students how to observe scientific phenomena related to the brain, behavior and mental illness, and to report them clearly in writing.
3. Research on better ways to communicate new knowledge and directions of scientific growth in the area of neuroscience and mental illness to teachers and curriculum developers.

For further information on pediatric translation research and treatment development topics, contact:

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Division of Adult Translational Research and Treatment Development (DATR)

The DATR is responsible for planning, directing and supporting programs of research, research training, research dissemination and resource development aimed at understanding the pathophysiology of mental illness and hastening the translation of behavioral science and neuroscience advances into innovations in clinical care. The Division supports a broad portfolio of pre-clinical and human clinical studies that focus on the phenotypic characterization and risk factors for major psychiatric disorders. In addition , the Division studies psychiatric disorders

of late life. The division is comprised of four branches. These branches are: The Adult Psychopathology and Psychosocial Intervention Research Branch, The Clinical Neuroscience Research Branch, the Geriatrics Research Branch and the Experimental Therapeutics Branch. Their respective functions are as follows:

Adult Psychopathology and Psychosocial Intervention Research Branch. This branch promotes the integration of basic behavioral and neuroscience findings into translational research on the foundations of psychopathology and functional disability. The branch targets new science based assessment, prevention, treatment and rehabilitation practices including research on causal risk and protective factors for mental disorders, mechanisms that convert vulnerability into psychiatric symptoms and disability and use of modern psychometric and statistical theories to advance nosology and assessment. Other specific areas of emphasis include mood, sleep and eating disorders, anxiety disorders and schizophrenia.

Clinical Neuroscience Branch. The focus of this branch is on the understanding of the neural basis of mental disorders. Human and animal studies are supported on the molecular, cellular and systems level of brain function designed to elucidate the pathophysiology of mental disease and to translate these findings to clinical diagnosis, treatment and prevention. These approaches are applied to the spectrum of mental disorders including schizophrenia, depression, bipolar disorder, anxiety disorder and other brain disorders. Areas of emphasis include: identification of valid and unique neurophysiological markers or complexes of markers for the major mental disorders and development of animal and or computational models that accurately mimic complex neurophysiology or behaviors characteristic of mental illness.

Geriatrics Research Branch. This branch focuses on research, research training and resource development in the etiology and pathophysiology of mental disorders of late life as well as the treatment and rehabilitation of persons with these disorders. Disorders studied include Alzheimer's disease and related dementias, psychotic disorders and schizophrenia, mood, anxiety and personality disorders, suicide, sleep disorders and eating disorders. Selected areas of emphasis include: development of more reliable and valid phenotypes, assessments and behavioral markers for late-life mental disorders,

Experimental Therapeutics Branch. This branch supports multidisciplinary research on novel pharmacological approaches to the treatment of mental disorders, evaluation of existing treatments of mental disorders, development and assessment of putative biomarkers of psychiatric disease and treatment response and development and testing of novel treatments. Studies supported include early phase clinical studies of new medications, studies to predict treatment response and studies to validate biomarkers or predictors of therapeutic response to pharmacological intervention. Side effects of therapeutic agents are also given emphasis. Programs exist to develop new treatments for psychotic disorders and also for mood and anxiety disorders.

All applications relevant to the mission of the Division of Adult translational Research and Treatment Development will receive full consideration. Possible areas for future research include:

A. ***Instrumentation for Clinical Research.*** Modern equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.

   1. *Physiological Monitoring*. Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for clinical research would include developing:

      a. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.

      b. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real time.

   2. *Development of Adult Physiological and Behavioral Measures*.

      a. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate,

galvanic skin response, and motor behavior).

b. Telemetry capability for non-invasive devices so that adults can be monitored for prolonged periods without interfering with their behavior.

c. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psycho-physiological measure(s) of interest.

d. Automated methods to detect specific emotional states using behavioral and autonomic indicators in adults.

3. *Behavior Monitoring and Analysis*.

a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.

b. Computer software to ease analysis of behavior monitored by video or telemetry systems.

B. ***Technologies for Adult Clinical Research.*** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer-based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.

1. *Assessment Tools*.

a. New technologies to assess and validate occurrence of and injuries resulting from physical and sexual abuse or from trauma as a result of terrorism or natural disaster

b. Technologies to assess CNS effects of psychosocial variables and interventions.

c. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

d. Computerized methodologies for assessing various mental disorders suitable for use in primary care settings.

e. Inexpensive methodologies or techniques for assessing adherence to medication regimens.

2. *Methodological Research and Development*. There is a need to devise new ways of data collection, analysis, management and dissemination.

a. New relatively culture-free taxonomies and/or measures of basic behavioral and social phenomena that can be employed in research across socio-cultural contexts.

b. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.

c. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.

d. Causal modeling methodology as applied to correlational longitudinal data sets.

e. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.

f. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.

g. Development of improved standardized instruments and methods for assessing assets, deficits, and disorders in adult and late life.

C. ***Adult Treatment and Preventive Intervention Research***

1. Development of novel methods to enhance efficiency of early phase clinical trails.

2. Development of novel assessments of psychopathology suitable for use in clinical research.

3. Identification of causal risk and protective factors for mental disorders.

4. Development of standardized assessments of psychiatric and comorbid disorders.
5. Develop psychometrically sound methods for assessing the cognitive, affective and behavioral response systems believed to underpin clinical symptoms and functional impairments.
6. Identify valid markers of illness onset.
7. Develop new definitions and measures to assess functioning in people with psychiatric disorders including self-reports, tests that simulate real-world tasks and new approaches to ratings by observers.
8. Creation and validation of new measures of functional capacity.
9. New approaches to assess the functional effects of drug or psychosocial interventions to treat mental disorders.
10. Identify valid and unique neuropsychological markers for the major mental and personality disorders.
11. Identify more reliable and valid phenotypes, assessments and behavioral markers for late-life mental disorders.
12. Development of techniques for maintaining or restoring mental capacities in older adults who experience declining learning and memory abilities due to age-related brain disorders.

D. ***Experimental Therapeutics Research.***

1. Early phase clinical studies of new medications targeting major mental illnesses or symptom domains now lacking adequate treatments.
2. Studies to validate new biomarkers or predictors of therapeutic response to pharmacological interventions.
3. Development of novel somatic treatments or medical devices for the treatment of mental illness.
4. Development of biomarkers or predictors of treatment response or side effects of therapeutics.
5. Development of new approaches to understand and predict the types, rates and pathophysiology of adverse effects of psychotropic medications.
6. New approaches to understand age-related changes on the emergence of adverse effects from psychotropic medications.
7. Development of new techniques to predict emergence of later abnormalities in body weight and disorders of glucose and lipid metabolism during treatment with psychotropic drugs.
8. New methods to predict and assess the effects of psychotropic medication on cerebrovascular and cardiovascular function.
9. New approaches, including pharmacological to prevent or reduce the negative metabolic, vascular and other side effects of psychotropic medications.

For further information on these topics, contact:

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Division of AIDS and Health and Behavior Research (DAHBR)

The DAHBR supports research and research training to develop and disseminate behavioral interventions that prevent HIV/AIDS transmission, understand and alleviate the neuropsychiatric consequences to HIV/AIDS infection and, using a public health model, supports studies to reduce the burden of mental illness from medical co-morbidities, non-adherence to treatment, stigma and health disparities. In addition to the topics listed below, the Center welcomes a wide range of applications dealing with HIV/AIDS prevention issues. Inquiries are encouraged. Examples of possible SBIR initiatives include:

A. ***Behavior Change and Prevention Strategies.*** To reduce HIV transmission especially among minority populations and hard to reach subsets of those populations.

1. Development of methods to reduce, prevent and/or change HIV-associated and STD risk behaviors.
2. Development of relapse prevention methods for HIV-associated risk behaviors.

3. Development of curricula for training clinicians and other health care practitioners in the prevention and treatment of HIV-related mental disorders.
4. Development of school-based curricula to promote HIV prevention by educators and teachers.
5. Development of HIV prevention materials to be used in community-based outreach programs for special populations (school dropouts, homeless, street youth, incarcerated youth).
6. Development of curricula for training in multicultural issues and development of cultural competence in HIV risk assessment, counseling, and prevention.
7. Development of print and/or computer based materials to assist primary care practitioners in informing their patients about HIV risk and prevention.
8. Development of innovative approaches to reduce stigma often expressed toward individuals with HIV/AIDS.
9. Development of materials and other programs to assist health care practitioners in improving patient adherence to medical and lifestyle regimens.
10. Development of low cost strategies to assist community-based organizations in using computers to educate hard to reach populations about HIV risk and prevention.
11. Development of strategies to assist organizations in identifying and implementing proven HIV prevention strategies and in addressing health disparities.
12. Methods to increase use of HIV testing and facilitate effective test result confirmation and counseling.
13. Development of new behavioral strategies to reduce high risk behavior among persons recently infected.

B. ***Neuro-AIDS: HIV-1 Infection and the Nervous System.***

1. Development of novel non-invasive (e.g., neuroimaging) approaches to assess and study mechanisms of neurologic and neurocognitive dysfunction associated with HIV infection.
2. Development of in-vivo and in-vitro models to assess mechanisms of HIV-1 trafficking into and out of the CNS, mechanisms of neuropathogenesis and therapeutic strategies for eradicating HIV-1 in the CNS.
3. Development of novel molecular markers for NeuroAIDS using proteomics, microarrays and neuroimaging.
4. Development of novel molecular approaches to study compartmentalized viral evolution in the CNS.
5. Development of improved anti-retroviral therapeutic strategies for targeting CNS infections including: facilitated entry of anti-retroviral therapeutic agents through the blood-brain barrier by manipulation of transporter systems and development of novel anti-retroviral therapeutic agents that readily pass through the blood-brain barrier.
6. Development of novel therapeutic approaches to block or reverse CNS dysfunction associated with HIV infection.
7. New approaches to reduce transmission risk or neuro-cognitive impairment in persons with recent HIV infection (0-6 months post exposure).

C. ***AIDS Mental Health Services Delivery.***

1. Video and computer-assisted methods to train health and mental health care providers in the psychosocial and neuropsychiatric aspects of HIV infection and AIDS.
2. Development of methods to assess functioning in families in which there is an HIV infection in order to develop improved treatment modalities.
3. Development of novel programs to train people infected with HIV in self-care management and identification of stress and development of improved coping strategies in order to improve quality of life.
4. Development of novel programs to help people recognize and seek treatment of mental health problems arising from living with HIV/AIDS as a long-term chronic condition.
5. Development of information, instruments or methodologies to improve and/or track adherence to complex HIV/AIDS drug

therapies for Hispanic and African American populations.

6. Development of innovative approaches to link researchers with community providers in the implementation of research-based HIV prevention efforts at the community level.

D. ***Health and Behavior Research.***

1. Development of behavioral strategies to assess mental health functioning and disability.
2. Research on identifying and addressing the sociocultural factors involved in mental health disparities.
3. Research on improving adherence to behavioral or pharmacological treatments.
4. Research on identification of risk factors for poor adherence.
5. Research on improved approaches to accurately identifying co-morbid disorders.
6. New approaches to improve the diagnosis and assessment of co-morbid physical and mental disorders.
7. Development and evaluation of new programs and strategies for self management and behavior change for persons with co-morbid mental and physical disorders.
8. New behavioral approaches to treatment of co-morbid mental and physical disorders in the elderly.
9. Development of new approaches to reduce stress in people with mental disorders.
10. Development of new approaches and strategies to reduce stigma directed at persons with mental disorders.

For further information on these topics contact:

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Division of Services and Intervention Research

The Division of Services and Interventions Research supports research, research demonstrations, research training, resource development, and research dissemination in prevention and treatment interventions, services research, clinical epidemiology, and diagnostic and disability assessment. The division is comprised of three branches: Services Research and Clinical Epidemiology Branch, Adult and Geriatric Treatment and Preventive Intervention Research Branch, and Child and Adolescent Treatment and Preventive Intervention Research Branch.

The Division supports two critical areas of research:

- Intervention research to evaluate the effectiveness of pharmacologic, psychosocial (psychotherapeutic and behavioral), somatic, rehabilitative and combination interventions on mental and behavior disorders-including acute and longer-term therapeutic effects on functioning across domains (such as school, family, peer functioning) for children, adolescents and adults.
- Mental health services research

The interventions focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, and the variety of community and institutional settings in which treatment is provided. It includes clinical trials evaluating the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with additional populations (such as women, ethnic and racial groups), new settings (public sector, pediatric primary care, schools, other non-academic settings, communities at large) and people with co-occurring disorders. Other foci include: identifying subgroups who may be more likely to benefit from treatment, evaluating the combined or sequential use of interventions (such as to extend effect among refractory subgroups), determining the optimal length of intervention, establishing the utility of continuation or maintenance treatment (that is, for prevention of relapse or recurrence), and evaluating the long-term impact of efficacious interventions on symptoms and functioning.

Services research covers all mental health services research issues, across the lifespan and disorders, including, but not limited to:

- Services organization, delivery (process and receipt of care), and related health economics at the individual, clinical, program, community and systems levels in specialty mental health, general health, and other delivery settings (such as the workplace).
- Interventions to improve the quality and outcomes of care (including diagnostic, treatment, preventive, and rehabilitation services.
- Enhanced capacity for conducting services research
- The clinical epidemiology of mental disorders across all clinical and service settings.

The Division also provides biostatistical analysis and clinical trials operations expertise for research studies; analyzes and evaluates national mental health needs and community research partnership opportunities; and supports research on health disparities.

During FY2006 SBIR grant priorities include:

1. **Clinical Trials Methodologies:** The development, testing and refinement of methodologies, instruments and statistical approaches to facilitate collaborative clinical trials for the prevention, treatment and rehabilitation of individuals with mental disorders; the development of innovative trials design (e.g., fixed adaptive, encouragement, partially randomized preference) the application of modern technology to enhance the science, operation, and management of multi-site mental health clinical trials; and the development of mental health clinical trial archives.
2. **Science Training and Education:** SBIR applications must focus on DSIR's research priorities. Develop, modify and test new and existing technologies, strategies and approaches to: (1) enhance science and research training across the educational/ career pipeline; (2) improve scientific literacy for clinicians and service/ organizational providers; (3) encourage entry and retention of individuals with non-mental health science backgrounds (engineers, computer scientists, medical anthropologists, law, business) or perspectives (individuals from under-represented communities) into the mental health services and interventions field; (4) keep established researchers and practitioners up-to-date on the findings, implementation, and methods of services and interventions research; and (5) facilitate *participatory* research with individuals, families and communities. This can include the development of science/ research education materials, curriculum, methodologies and web-based programs relevant to the mission of the division; the development of networking and collaborative approaches to research training in mental health interventions and services research; and the development of multi-media approaches (combined with traditional strategies) to improve the level of scientific and career mentoring that mental health services and interventions researchers receive.
3. **Public Health Oriented Pharmacoeconomics:** Develop and test simulation models for estimating the amount of total out-of-pocket expenditures (co-payments) for the most frequently prescribed psychotropic drugs under different insurance benefit scenarios and/or under different pharmacy benefit management scenarios. Models should also be developed to accommodate common combined pharmaceutical approaches.
4. **Dissemination:** Development of technological approaches to increase the sustainable uptake of scientifically based treatments and services across diverse community settings. This could include web-based interactive tools for state/county mental health or related (e.g., schools) agencies around implementation of evidence-based practices. Development of innovative ways (e.g., new technology, use of multi-media) of disseminating information to stakeholders. Development of new approaches to the dissemination and implementation of evidence based mental health interventions to underserved populations (e.g., rural/frontier, aging individuals with neuropsychiatric disorders).
5. **Implementation:** Application of new technologies, approaches and strategies to

identify and utilize active therapeutic ingredients in complex community-based services and programs that optimize functioning and sustain community reintegration of people with mental disorders. Use of technologies and strategies to assist service systems to more adequately plan for transitions (e.g., child to adult system, prison to community) and seamlessly integrate mentally ill individuals moving between these sectors.

6. **Merging Multiple Data Sets:** Merging multiple data sets (e.g., claims, trials, pharmacy etc.) for innovative and complex analytic strategies.

7. **Community Outreach to Diverse and Underserved Populations:** Application of new technologies and strategies to develop, test, and refine culturally appropriate materials and approaches to: (a) foster help-seeking and engagement of diverse and underserved populations in research-based mental health treatment and prevention; to foster participation in community based research by diverse and underserved populations; and to inform diverse provider groups about state-of-the-art mental health treatments and services in order to facilitate their implementation of these interventions.

A. ***Services Research and Clinical Epidemiology Branch.*** The branch supports research on the organization, financing, delivery, effectiveness, and appropriateness of mental health care in everyday settings in order to find ways to improve the effectiveness, efficiency, and equity of mental health services (including preventive services) in community and other settings. Also supported are studies on pharmacoeconomics, pharmaco-epidemiology, and the distribution, determinants, and course of mental illness in the context of various clinical settings. Mental health services include mental health care provided in specialty mental health and general health care settings, including primary care, hospitals, nursing homes, and other residential care settings, as well as in educational settings and various legal system settings, such as jails, juvenile detention and correctional facilities, prisons, and probation and parole programs. Other services often needed by mentally ill persons include social services, vocational and rehabilitation services, welfare, and housing. Relevant services include those provided to children and adolescents with emotional disorders, adults and elderly adults with mental disorders, and persons with mental illness that co-occurs with physical illness and with alcohol and/or drug abuse disorder. Research methodologies include ethnographic studies, surveys, and analyses of secondary data, randomized controlled trials, quasi-experimental designs, cohort, and case-control studies.

Advances in clinical epidemiology, mental health treatment and services research fields have made it imperative that intensive work continue in the areas of assessment/screening technologies, outcome assessment measurement and measurement packages, dissemination technologies, data analysis techniques, and the training of clinicians and providers. The translation of efficacious and effective treatments into primary care, community mental health centers, and managed care settings is both a major challenge and opportunity to develop technologies and systems that will improve the care and rehabilitation of patients and enable them to profit from the research advances that have been made. Research is needed on the dissemination of empirically supported treatments or services.

1. *Methodological Research Program*. Supports studies that involve development, testing, and refinement of methodologies and instruments to facilitate research on services for mentally ill persons, including measures of severity of illness, family burden, social support, quality of care, effectiveness of care, direct and indirect cost of mental disorders, and short-term and long-term outcome measures; studies submitted by statisticians, psychometricians, and other experts in research methodology and scientific data analysis for work on the design, measurement, and statistical challenges inherent in conducting mental health services research.

2. *Outcomes and Quality of Care Research*. This program is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral sciences in general. The program supports

research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services.

3. *Systems Research Program*. Supports studies on organization, coordination, and collaboration of mental health and related services both within and across care settings in order to improve mental health outcomes and prevent or treat co-occurring substance abuse, physical problems, and other behavioral health disorders. Service sectors of interest include: the criminal justice system, housing and other social services, community support, post-trauma services, and adult autism services. Also relevant are studies to establish the effectiveness of legal mechanisms relevant to persons with mental illness, such as outpatient commitment, community monitoring, and guardianship; and the development of the role and expertise of social workers in mental health research activities.

4. *Disparities in Mental Health Services Program.* Plans, stimulates, disseminates, and supports research on the complex factors that influence disparities in mental health services, particularly across special population groups such as racial and ethnic groups, as well as women and children, and persons living in rural and frontier areas. The program addresses care delivered in a variety of settings such as the specialty mental health sector, the general medical sector, and community settings (such as schools). Also, it supports research that examines innovative services interventions (such as community-based participatory methods, faith-based) to overcome mental health disparities related to mental health service delivery and use.

5. *Sociocultural Research Program*. Is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral sciences in general. The program supports research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services.

6. *Child and Adolescent Services Research Program*. Includes research on the quality, organization, and content of services for children with mental disorders and their families. The program focuses on child mental health services provided in multiple sectors and settings, such as schools, primary care, child welfare, juvenile justice, and mental health. Program emphases include practice research within child service systems, research testing the outcomes of innovative child service delivery models, and studies that examine the adaptability or sustainability of child mental health services.

7. *Financing and Managed Care Research.* Supports research on economic factors affecting the delivery of mental health services including the economic burden of mental illness; financing and reimbursement of public and private mental health services; impact of various forms of managed care and physician payment methods on the cost of mental health care; pharmaco-economics; evaluation of the impact of insurance coverage including mandated coverage and mental health insurance parity on access, cost, and quality; cost-benefit, cost-effectiveness and cost-utility analysis of mental health service interventions; and economic analysis of practice patterns of different mental health providers. The goal of the program is to expand understanding of the role of economic factors in the delivery and use of mental health services and assist in the development of improved mental health financing methods promoting high quality, cost-effective care for people suffering from mental disorders.

8. *Primary Care Research*. Includes studies on the delivery and effectiveness of mental health services within the general health care sector; recognition, diagnosis, management, and treatment of mental and emotional problems by primary care providers; coordination of general medical care with and referrals to mental health specialists; provision of psychiatric emergency services, consultation/liaison psychiatry, and other psychiatry, psychology, and social work services within

the general medical care sector; studies that improve understanding of how best to improve care for people with mental disorders and co-occurring physical conditions.

9. *Clinical Epidemiology Research*. Includes epidemiologic studies of mental disorders in clinical settings, that is, the distribution of treatments and services in a population; studies to determine usual or best practices and the relationship to patient, provider, and system factors, as well as to outcomes; pharmaco-epidemiology studies; research to identify factors for the development of mental disorders in clinical settings, factors important in the natural history of mental disorders, including comorbid conditions, and the rates of occurrence of mental disorders in clinical and services populations.

10. *Disablement and Functioning Research Program*. Supports studies on the development of methodologies for assessing disablements and functional status, and the development of global and specific measures of disablements and functional status; the identification and assessment of disablements/functional status in clinical investigations and in clinical epidemiological surveys. In addition, it supports studies of the relationship of rehabilitative and traditional mental health services and service systems; impact of disability benefits and insurance; factors affecting impairments and disabilities during and as an outcome of rehabilitation and other treatments; rehabilitative services focused on specific domains of disabilities, such as work and social relationships; and, factors that influence and sustain community reintegration.

11. *Dissemination and Implementation Research Program.* Includes studies that will contribute to the development of a sound knowledge base on the effective transmission of mental health information to multiple stakeholders and of the process by which efficacious interventions can be adopted within clinical settings. Research on dissemination will address how information about mental health care interventions is created, packaged, transmitted, and interpreted among a variety of important stakeholder groups. Research on implementation will address the level to which mental health interventions can fit within real-world service systems. Related topics include multilevel decision-making perspectives about services and interventions in community settings, with special focus on translating behavioral science into applied research in these areas.

B. ***Adult Treatment and Preventive Interventions Research Branch.*** This Branch supports research evaluating the therapeutic (acute, maintenance, and preventive) and adverse effects of psychosocial, psychopharmacologic, and somatic interventions of proven efficacy in the treatment of mental disorders in adults. It includes trials evaluating and comparing the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with specialized populations (such as women, or specific ethnic or racial groups), new settings (public sector, or computer based), new methods of treatment delivery (e.g., web or computer –based), and people with comorbid physical or mental disorders.

1. *Somatic Treatments Program.* Areas include electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (RTMS), bright light, physical exercise, and similar nonpharmacologic approaches for which efficacy has been demonstrated.

2. *Adult Psychotherapy Intervention Program.* Areas of program responsibility include evaluation of the effectiveness of psychotherapeutic, behavioral, and pspychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and applications of psychotherapy treatments.

3. *Adult Psychopharmacology Intervention Program.* Areas of program responsibility include research involving psychotropic medications of demonstrated efficacy. Examples include evaluation of long-term effectiveness of pharmacotherapy and treatment of subpopulations of recognized diagnostic groups.

4. *Adult Integrated Treatment Program.* Areas of program responsibility include the use of combined or sequential treatment approaches to improve long-term outcome.

A major focus is improvement of efficacious psychopharmacological interventions to maximize symptomatic relief while minimizing adverse reactions. For example, medications may be combined with the full range of therapies in individual, conjoint, or group settings.

5. *Preventive Interventions Program.* Areas of program responsibility include studies evaluating the effectiveness of preventive interventions, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (such as prevention of relapse, recurrence, inappropriate resource use) or side effects. A specially designated programmatic focus is the area of suicide prevention.

6. *Rehabilitative Interventions.* Areas of program responsibility include evaluation of the effectiveness of psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and applications of psychotherapy.

C. ***Child and Adolescent Treatment and Preventive Intervention Research Branch.*** The branch supports research to evaluate the effectiveness of mental health preventive, treatment and rehabilitative interventions- alone or in combination-for children and adolescents (including those co-occurring with other conditions). The Branch also supports research addressing the long-term effectiveness of known efficacious interventions, including their role in the prevention of relapse and recurrence of mental disorders.

Areas of emphasis include: Research on the effectiveness of treatment interventions for childhood and adolescent mental and behavioral disorders in practice and community settings to determine the real life therapeutic benefit short-and-long term; Research to prevent mental and behavioral disorders in children and adolescents; Research to build new methodologies that can be effectively used to evaluate the safety of interventions in community settings; Research to determine whether treatment of mental and behavioral disorders in children results in improved outcomes as adolescents and young adults and prevents the negative functional outcomes associated with those disorders (such as substance abuse, academic failure, higher medical costs, co-occurring mental disorders). juvenile justice facilities.

1. *Pharmacologic Treatment Intervention Program.* Areas of program responsibility include evaluation and comparison of efficacious pharmacological and other somatic treatments for children and adolescents with mental disorders.

2. *Combined Intervention Program. Child and Adolescent Combined Intervention Program.* Areas of program responsibility include all research that combines different treatment modalities in which efficacy has been demonstrated in a single combined or comparative protocol.

3. *Psychosocial Intervention Program.* Supports research evaluating the effectiveness of psychosocial interventions on children's and adolescents mental and behavior disorders, including acute and longer-term therapeutic effects on functioning across domains. It includes trials evaluating the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with additional populations, new settings, and people with comorbid disorders.

4. *Preventive Intervention Program.* Areas of program responsibility include research examining the effectiveness of preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems with asymptomatic subclinical populations.

For further information on Services and Intervention Research contact:

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NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The mission of NINDS is to reduce the burden of neurological disease—a burden borne by every age group, by every segment of society, by people all over the world. To this end, the Institute supports and conducts research on the healthy and diseased brain, spinal cord, and peripheral nerves. Hundreds of disorders afflict the nervous system. Common killers and disablers such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke, epilepsy, and autism are well known. Other disorders we study may be known only to the patients and families affected, their doctors, and scientists who look to rare disorders for help in understanding the brain as well as treating more common diseases.

Phase II Competing Renewal Awards

NINDS will accept Phase II SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require approval of a federal regulatory agency. Such products include, but are not limited to: medical implants, drugs, biologics, and new treatment or diagnostic tools that require FDA approval.

NINDS will accept applications for up to three years that do not exceed $750,000 per year in direct costs or $1,000,000 per year in total costs.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II Competing Renewal projects. This list is not meant to be all-inclusive, and applications for other appropriate activities will be accepted.

1. Studies for preclinical discovery and development of drugs to treat neurological disorders, including pharmacology and toxicology studies, beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development .
2. Completion of studies as required by the FDA for an IND application.
3. Human clinical trials/studies to determine the safety profile, metabolism, and/or efficacy of a drug.
4. Safety and effectiveness studies of novel medical devices.

Please contact Dr. Randall Steward (contact information provided below) before beginning the process of preparing an application. Prospective applicants are strongly encouraged to submit a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-06-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NINDS SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

Any Phase II Competing Renewal applications that do not propose to develop products that require regulatory approval, or that exceed the direct or total cost budget caps, will be withdrawn from consideration prior to peer review.

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Examples of research topics within the mission of the NINDS that may be of interest to small businesses are shown below. For additional information about areas of interest to the NINDS, please visit our home page at http://www.ninds.nih.gov.

Extramural research is organized in the following programmatic areas within NINDS: neurodevelopment, neurogenetics, repair and

plasticity, systems and cognitive neuroscience, channels, synapses and circuits, neurodegeneration, neural environment, and technology development. Specific areas of interest are listed below:

Neurodevelopment

A. Development of computer software to permit reconstruction of magnetic resonance imaging (MRI) from unrestrained patients or animals that may change position within the MRI magnetic field.

B. Development of technology to assess fetal neurological integrity such as fetal MEG.

C. Non-invasive monitoring of brain function such as improvements in PET imaging, MRI imaging and spectroscopy, and methods of optical imaging such as development of near infrared spectroscopy (NIRS) for monitoring of changes in cerebral oxygen saturation, cerebral blood flow and volume, and oxygen utilization in the brain, and for functional imaging utilizing scattering and absorption characteristics of brain tissue.

D. Non-invasive techniques for structural imaging, such as near infrared imaging.

E. Development of computerized histological tomographic brain atlas graphics, which can be stored and manipulated on a personal computer for teaching, research data modeling and display, and correlation with clinical neuroimaging.

F. Development of practical imaging modalities in extremely ill very low birth weight infants.

G. Non-invasive techniques for assessment and continuous bedside monitoring of cerebral function in the neonate, such as, but not limited to, functional near infrared spectroscopy and amplitude-integrated EEG.

H. Development of improved technology for MRI imaging of infants and small children, for example, specially designed pediatric sized head coils, or devices to minimize movement artifact in unsedated infants.

Neurogenetics

A. Analysis of central nervous system cell lineages for treatment of neurodevelopment and degenerative disorders.

B. Development of embryonic stem cell models of nervous system development and function.

C. Development of technology for the production of high quality cDNA libraries from small tissue samples of the brain during development and in response to disease, injury or pharmacological agents.

D. Identification of optimal DNA vector systems to standardize and expedite the sequencing of cDNA libraries derived from micro dissected brain tissues.

E. Development of technology for micro dissection of brain tissue for single cell analysis of gene expression.

F. Development of informatics systems to expedite the analysis and use of sequence data that will be derived from projects to identify novel genes and to map temporal and spatial dimensions of gene expression in the brain.

G. Development of proteomics technologies to quantitatively detect levels of expression, post-translational modifications, and subcellular distribution of proteins in the nervous system.

H. Development of technology to detect and quantify metabolite (carbohydrates, lipids, peptides) changes in the nervous system.

I. Development of in vitro methods to either fractionate membrane proteins or express recombinate membrane proteins at sufficient levels for proteomics analyses.

J. Development of technology for single-cell analysis of neurons and glia to detect dynamic changes in the transcriptome, proteome, and metabolome.

K. Development of methodologies to deliver therapeutics (gene vector, drugs, enzymes) across the blood-brain-barrier.

L. Improved methodologies for creating transgenic animal models for diseases in the nervous system.

M. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of CNS tumors.

N. Advancement of molecular analysis of DNA, RNA and protein in CNS tumors.

O. Surrogate markers for cerebrovascular, immune, and infectious diseases and CNS tumors.

P. Develop methods for identification of specific neural cell lineages.

Q. Techniques for brain specific antisense, gene and protein transfer into cerebrovascular, neurons, or glial cells in brain tumors.

R. Methods to deliver brain specific proteins and genes through the blood-brain and blood-CSF barriers for targeting CNS tumors.

S. Mass spectrometry for the analysis of protein in the CNS and in brain tumors.

T. Highly specific radiolabeled markers for different types of brain tumors that can be used under histopathological or brain imaging conditions.

U. Development of an intracranial pressure monitor.

V. Refinement of functional, structural and metabolic imaging techniques for brain tumors.

W. Methods and devices for high throughput genomic and proteomic expression and data analysis in brain tumor.

X. Improved methods to deliver neurotrophic factors and other small proteins or peptides normally found in the brain.

Repair and Plasticity

A. *Neural Prostheses and Deep Brain Stimulation*.

1. Design, development, and evaluation of neural recording and stimulating microelectrodes for neural prostheses and deep brain stimulation.
2. Development of thin, insulating coatings to make implanted electronic packages impervious to the corrosive action of body fluids and tissues.
3. Development of transducers of position, touch, and force for use in functional electrical stimulation systems.
4. Development of addressable arrays of sub-micron or nano-scale dimension electrodes for use in the CNS.
5. Non-invasive methods to focally stimulate small populations of neurons within the body.
6. Development of communication aids for individuals with “locked-in syndrome.”
7. Development of a complete system utilizing existing microelectrodes, lead wires and telemetry to transfer neural signals outside the body.
8. Develop new high charge density electrode materials.
9. Development of a method to repeatedly inhibit neuronal electrical activity in a safe and effective manner.
10. Development of a non-invasive method of selectively stimulating and/or inhibiting small groups of nerve fibers within a nerve trunk.
11. Development of materials to minimize scarring following surgery in the central nervous system.
12. Development of techniques for precise functional placement of microelectrodes within the central nervous system.
13. Development of neural controllers to restore micturition and defecation for individuals with spinal cord lesions.
14. Development and implementation of automated signal processing algorithms in hardware or software capable of neural signal analysis for neural prosthetics applications.
15. Development of novel nerve cuff electrode or nerve interface technologies capable of selective stimulation and/or recording from intact afferent and efferent nerve bundles.

B. *CNS Trauma and Rehabilitation*.

1. Means of assisting or achieving restitution of function after injury to the nervous system.
2. Develop transgenic, knockout and inducible knockout animal models for stroke and CNS trauma research.
3. Develop technology for data gathering and analysis for assessment of multiple parameters of ICU recording in brain trauma.
4. Develop instruments or techniques to enhance monitoring of nervous system activity during surgical procedures, aimed at improving the safety, targeting or efficacy of those procedures.

5. Develop new preclinical testing for promising therapies for acute and chronic central nervous system injury.
6. Establishment of networks to test pharmaceutical agents in animal models of CNS trauma.
7. Development of monitors for such modalities as intracranial pressure, brain temperature, and cerebral blood flow.
8. Develop drugs or other agents to reduce scarring after spinal cord injury.
9. Develop and test novel biological assays for use as diagnostics in acute stroke (ischemic vs. hemorrhagic), traumatic brain injury, and spinal cord injury.

C. *Neuroimaging*.

1. Development of ultrasound imaging methods for the central nervous system.
2. Develop methods and reagents that allow tracking of grafted cells in the living host animal using non-invasive imaging methodologies.
3. Development of imaging techniques to track the course of injury and repair following spinal cord injury.

D. *Stem Cell Biology*.

1. Development of a website and database for posting and discussion of protocols and best practices used in harvesting, maintaining in culture, and inducing differentiation of stem cells.
2. Development of a stem cell repository for the storage of stem cells from different sources and immortalized cell lines, and for making these reagents readily available to the research community.
3. Develop efficient and reproducible methods for harvesting and storing stem cells for research use.
4. Develop markers, reagents, and new methodology for the identification and/or harvesting of stem and progenitor cells in the nervous system and in other tissues.
5. Develop methods for phenotyping stem and progenitor cells in the nervous system.
6. Use of mutant and transgenic mice or rats to study the effect of identified genetic alterations on neurogenesis in the adult central nervous system.

E. *Axonal Regeneration/Guidance and Synapse Formation*.

1. Develop biomaterials to serve as paths for supporting or guiding axonal growth across a site of injury.
2. Develop methods to deliver neurotrophic factors, cells or genes to injured brain sites to enhance regeneration or restoration of function.
3. Develop biomaterials to promote sprouting and directed growth of axons toward specific sites in the central nervous system.
4. Develop biomaterials to promote dendritic growth and stability, and synapse formation in localized areas.

Systems and Cognitive Neuroscience

A. *Cognitive and Behavioral Neuroscience*.

1. Development of computerized neuropsychological assessment tools to facilitate testing of neurologically impaired subjects.
2. Development of techniques and devices for imaging of small animals such as transgenic and knockout animal models of complex behaviors.
3. Design, development, and evaluation of automated systems for assessment of behavioral parameters.
4. Development of computer software that integrates imaging and physiological measures of brain activation.

B. *Sleep Neuroscience*.

1. New therapies for sleep disorders.
2. New methods to categorize sleep stages on line – especially in human infants and patients with EEG-distorting brain dysfunction.
3. New methods for quantifying optimal alertness.
4. Models of neurological sleep disorders.
5. Novel applications of evoked potentials to sleep neuroscience.

6. Further development of portable devices that facilitate cost-effective screening for potential sleep disorders, and can be used to monitor the progress of already diagnosed sleep disorders.
7. Applications of proteomic and/or metabalomic methods to detect sleep deprivation.

C. *Pain*.

1. Development of objective methods for quantitative assessment of pain, including development of a quantitative sensory testing battery for pain patients.
2. Development of novel pain model systems, particularly more accurate pre-clinical experimental models.
3. Development of tools to elucidate potential analgesic targets, and models for testing and validating these for efficacy in patients.
4. Development of new diagnostic tools for different pain mechanisms and objective measures of analgesic drug action.

D. *Neuroimaging*.

1. Development of devices for artifact-free monitoring of vital neurological parameters during MRI procedures involving very high static and dynamic magnetic fields (greater than 2 Tesla) and high-energy microwave radiation typical of the MRI environment.
2. Development of functional imaging techniques.
3. Development of combined imaging strategies, i.e., fMRI and PET.

Channels, Synapses and Circuits

A. *Epilepsy*.

1. Devices for automated detection and quantification of seizures.
2. New therapies both for the control of seizures and for the prevention of the development of epilepsy.
3. New formulations and delivery systems for antiepileptic drugs.
4. New models of seizures and epilepsy useful for screening therapies.
5. Improved methods of monitoring compliance/medication dispensing.

B. *Muscular Dystrophy*

1. Development of minimally invasive diagnostic techniques for the muscular dystrophies.
2. Development and validation of the role of muscle imaging in diagnostic evaluation or as a endpoint measure for clinical trials in muscular dystrophy.
3. Evaluation of the efficacy of existing anti-inflammatory drugs for treatment of muscular dystrophy.
4. Therapeutic drug discovery for the range of muscular dystrophies.
5. Development of assistive devices for individuals with muscular dystrophy.
6. Development of standardized instruments to measure quality of life, cognitive, and central nervous system function for individuals with muscular dystrophy.
7. Development of optimized models for mechanistic studies of specific muscular dystrophies, including models appropriate for therapeutic development screens.
8. Development of cell-based assays that target aspects of pathogenesis and pathophysiology in the muscular dystrophies, to enable high throughput drug screening.
9. Development of high-throughput, small molecule screening efforts for promising therapeutic targets and identify novel targets for drug development
10. Determine the benefits and risks of varied exercise approaches in muscular dystrophies and develop scientifically based recommendations concerning optimal exercise, physical activity, and recreation.
11. Development of strategies to improve vocational outcomes and reduce social isolation of patients with muscular dystrophy.

Neurodegeneration

A. Development and preliminary testing of instruments, devices, or drugs that enhance diagnostic, treatment, or monitoring capabilities.

B. Identification or development of animal models for research on neurodegenerative disorders.

C. Development of early or presymptomatic diagnostic procedures for neurodegenerative disorders.

D. Epidemiology of neurodegenerative disorders.

E. New delivery methods of medications for degenerative neurological disorders.

F. Development of cell lines for in vitro modeling of neurodegenerative disorders.

G. Therapeutic drug discovery targeted to neurodegenerative disorders.

H. Development of drug screening assays, including biochemical, cellular or model organism assays for high-throughput screening approaches.

Neural Environment

A. *Infectious and Immune Disorders*.

1. Development of therapies to prevent, arrest or reverse autoimmune neurological disorders such as multiple sclerosis.
2. Development of methods that aid the diagnostic of infectious and immune disorders.
3. Development of methods or vectors for the delivery of biologics (e.g., cytokines, DNA), drugs, and other agents to the nervous system.
4. Development and studies of drugs with high blood brain barrier permeability intended for treatment of CNS infections including HIV-related opportunistic infections.
5. Development of animal models for infectious and immune disorders (e.g., k.o. or transgenic mice, viral systems) that allow the study and identification of the effect and contribution of genes to disease.
6. Development of techniques such as microarray, gene expression analysis or immunological techniques that allow the study and identification of the effect and contribution of genes to disease or the effect of therapies.
7. Development of techniques such as microarray, gene expression analysis or immunological techniques that allow studies on the mechanisms and effect of therapies.
8. Development of functional and other imaging techniques and tools, and of combinations thereof.
9. Development and evaluation of biomarkers for infectious and immune disorders.

B. *Stroke*.

1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of stroke patients.
2. Methods for the analysis of protein expression in the ischemic CNS.
3. Develop and validate large and small animal models, including transgenic, knockout, and inducible knockout animal resources, that reflect the complexity and diversity of the human brain and its responses during ischemia.
4. Brain specific gene and protein transfer methods that target cerebral vessels, neurons, and/or glia in the ischemic CNS.
5. Methods and devices for high throughput genomic and proteomic expression and data analysis in stroke.
6. Methods to transiently suppress gene and protein expression in brain ischemia.
7. Expand brain imaging capabilities to include new methods of imaging, synthesis of radiolabeled ligands for specific receptors, and refinement of functional, structural and metabolic imaging techniques.
8. Develop bioinformatic databases for stroke to include sharing of clinical, genomic, and/or proteomic data.
9. Identify biomarkers for vascular, inflammatory, and immune diseases of the brain.
10. Develop and test combination therapies for stroke.
11. Develop instruments, devices, and methods to enhance drug delivery through the blood-brain barrier.

C. *Prion Diseases*.

1. Development of a rapid and sensitive assay for the detection of normal and variant prions as well as the detection and isolation of various prion strains.
2. Transgenic, knockout and inducible knockout animal resources for Transmissible Spongiform Encephalopathy research.

Technology Development

A. Animal models, including genetic and experimental models of neurological disorders; examples include mouse mutants, models of spinal cord injury or traumatic brain injury, epilepsy, and channelopathies.

B. Neuroinformatics, including relational software for genetic, functional, and anatomical data; databases; and websites for data sharing.

C. Computational tools for understanding both cellular and systems level function in the nervous system.

D. Approaches to recording and stimulating neural activity, including single cells, cellular ensembles, and brain regions or fiber tracts.

E. Imaging tools, including MRI, fMRI, MRS, PET, MEG, optical and infrared, and ultrasound, both for human and animal studies.

F. Approaches to identify and characterize genes involved in function and pathology in the nervous system, including microarrays, genetic linkage methods, mutagenesis, expression analysis, and in situ localization.

G. Approaches to identify and characterize proteins involved in function and pathology in the nervous system, including electrophoretic, immunochemical, and mass spectrometric analyses.

H. Therapeutic drug discovery, including the development of molecular, cellular, or animal-behavioral screening assays; high-throughput screening approaches; and preparation of drug candidate chemicals or chemical libraries by traditional or combinatorial chemical approaches.

I. Bioengineering, including neural prostheses.

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NATIONAL INSTITUTE OF NURSING RESEARCH (NINR)

The National Institute of Nursing Research (NINR) supports research focused on biological and behavioral aspects of critical health problems that confront the Nation. Emphasis is on seeking ways to reduce the burden of illness and disability by understanding and easing the effects of acute and chronic illness, improving health-related quality of life by preventing or delaying the onset of disease or slowing its progression, establishing better approaches to promote health and prevent disease, and improving clinical environments by testing interventions that influence patient health outcomes and reduce costs and demand for care.

For additional information about areas of interest to the NINR, please visit our home page at http://www.nih.gov/ninr/.

Research and Development of Technologies for Health Promotion and Alleviation, Adaptation to, or Management of Symptoms

A. Technologies to be used in the hospital, long-term care, hospice, assisted living facility, or home setting that improve symptom evaluation in persons with chronic conditions. Conditions of interest include congestive heart failure, cystic fibrosis, organ failure, cognitive impairment, renal disease, asthma, diabetes, or mobility impairments.

B. Devices that improve the acceptance and use of assistive and monitoring devices, e.g., child peak flow measurement in the home and at school; nightly use of continuous positive airway pressure (CPAP).

C. Devices to diagnose and screen for COPD early in the course of the disease, particularly targeting young adults.

D. Technologies to assist in adolescent health promotion and prevention activities such as smoking cessation devices or obesity prevention technologies.

E. Devices to assist in providing palliative care for patients with life threatening illnesses through the disease trajectory whether in active treatment or at the end of life.

F. Technologies to assist individuals in reducing environmental exposures, i.e., chemical and viral agents, and indoor/outdoor allergens.

G. Devices to facilitate resource sharing such as: technologies that will enable valid and reliable measurement tools/instruments to be readily available and shared by research scientist focused on similar issues in a variety of populations.

H. Adaptation of existing or development of new technologies that will link under-represented populations with available resources to sustain healthy life styles and eliminate health disparities.

Research and Development of Technologies to Enhance Self Care and Clinical Care

A. Technologies to assist patients to adhere to chronic regimens such as reminding children to take steroid inhalers during the day for asthma; alerting obese adults when high calorie and fat content foods are about to be eaten; adhering to medication regimens; and prompting sedentary adults to exercise.

B. Devices that improve delivery of care to persons who have restricted or impaired movement due to (1) conditions of neurological disease or injury, peripheral vascular disease, rheumatoid disease, or intractable pain, (2) life sustaining equipment, such as dialysis machines or left ventricular assist devices, or (3) orthopedic fixation devices.

C. Devices to enable providers and or research scientists to monitor successful adherence to complex medication regimens (e.g., Highly Active Anti-Retroviral treatment).

D. Technologies that monitor short and long term self-care behavior changes.

E. Biological and behavioral monitoring devices for patients in at-risk and underserved populations in rural and frontier areas that will enable access to clinical care.

F. Telehealth technologies to improve patient outcomes through increasing quality, type, and speed of health information sharing, e.g., assessing traumatic injury severity at remote sites and transmitting this information to acute care settings for assessment and evaluation; communicating signs and symptoms of clients at home to health care providers in distant locations; tailoring care for diverse patients in a wide variety of settings, and promoting community interventions to eliminate health disparities.

G. Technologies to treat chronic wounds that fail to heal, specifically decubitus ulcers, venous stasis ulcers, and diabetic ulcers.

H. Technologies to be used in the hospital or home care setting to monitor or assess preterm, low-birth weight or other high-risk infants.

I. Technologies to assist informal caregivers in providing care or assistance to family members in the home.

J. Noninvasive devices to assess exposure to chemical and viral agents for children and adults and transmit this information to health care personnel for assessment and evaluation.

K. Technologies to disseminate research information (i.e., biobehavioral responses, communication of risk, bioethics) to nurses practicing in emergency settings and in the community.

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NATIONAL CENTER FOR RESEARCH RESOURCES (NCRR)

NCRR supports primary research to create and develop critical resources, models, and technologies. NCRR funding also provides biomedical researchers with access to diverse instrumentation, technologies, basic and clinical research facilities, animal models, genetic stocks, and more. These resources enable scientific advances in biomedicine that lead to lifesaving drugs, devices, and therapies.

For additional information about areas of interest to NCRR, please visit our home page at http://www.ncrr.nih.gov.

Research and Development in Instrumentation and Specialized Technologies for Biomedical Research

A. New or improved instruments, devices, and related methodologies to facilitate biomedical or behavioral research. Instrumentation includes but is not limited to mass spectrometry, nuclear magnetic resonance, fluorescent or kinetic or laser spectroscopies, X-ray absorption/ diffraction, electron or confocal microscopies, and flow cytometry.

B. Development of computer science/technology to study biomedical or behavioral research problems, e.g., computer visualization, computer modeling/simulation, structure-based drug design. Development of new bioinformatics technology infrastructure such as data management and analysis tools, networking infrastructure and collaborative tool development.

C. Development of novel technologies for proteomics and glycomics discovery, e.g., sample handing, separations, mass spectrometry, and computational tools for protein identification, data curation and mining.

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Research and Development in Comparative Medicine

A. Development of improved reagents and cost-effective methods to accurately screen and diagnose selected laboratory animal diseases, and for performing overall assessments of animal quality and health status. An urgent need currently exists for the development of improved methods for the detection of active tuberculosis in nonhuman primates.

B. Development of improved reagents and techniques for isolating and propagating embryonic stem cells (ESC), as well as fetal and adult stem cells from laboratory animals. Improved methods for causing ESC and other types of animal stem cells to differentiate along specific pathways in vitro and in vivo.

C. Development of improved reagents, techniques, and equipment for isolating, propagating and characterizing specific gene sequences cloned in bacterial artificial chromosome (BAC) vectors and for preparing and characterizing BAC libraries made from laboratory animals.

D. Development of improved reagents, techniques and equipment for preparing and analyzing full-length cDNA libraries made from tissues or cells of laboratory animals.

E. Development of new technologies to rapidly phenotype large number of mutant animals.

F. Development of vaccines and new therapeutic agents for the prevention and/or control of selected laboratory animal diseases. One high priority need is for the development of methods to control and prevent Herpesvirus B in nonhuman primates.

G. Development of commercially valuable reagents for lower organisms or established cell cultures.

H. Development of cost-effective methods for culture and/or preservation of commercially valuable organisms, including specific types of bacteria and other microorganisms.

I. Development of cost-effective husbandry and colony management techniques, equipment, and/or new approaches to improve laboratory animal welfare and assure efficient and appropriate research use.

J. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control.

K. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies on various types of human disease. A need exists for a small animal model of Hepatitis C virus infection in humans.

L. Development and refinement of new technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.

M. Development of improved reproductive biology techniques (e.g., cloning techniques; embryo splitting) to produce genetically identical laboratory animals.

N. Development of technologies for improved embryo transfer within a single animal species or of intraspecific embryo transfer to allow preservation of rare, unique, or endangered animal species that may have unique value as animal models for human disease.

O. Development of improved reagents, techniques, and equipment for performing and analyzing the results of microarray experiments.

P. Development and refinement of technologies for the analysis of regulation of gene expression in a wide range of model organisms, including non-mammalian species.

This could be accomplished by genetic means (e.g., transgenesis, conditional knock-out or knock-in) or epigenetic means (e.g., morphilinos, RNAi).

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Clinical Technology Applications

A. Development of patient-oriented research technologies. This includes therapies, diagnostics, sensors, and imaging technologies used for patient diagnosis, monitoring, and treatment.

B. Diversification of methods used for clinical studies of disease states, such as micro-analytical sensors or imaging devices.

C. Miniaturization of existing biomedical technologies for adaptation to pediatric use.

D. Development of artificial tissues and organs for medical use. Development of transplant technologies and human cell isolation techniques.

E. Development of vehicles for drug delivery, including for patient groups with a potential for altered pharmacology or compliance, such as children or the elderly.

F. Development of bioinformatics technology: (1) collection, collation, and archiving of databases; (2) assuring compatibility with other databases; (3) protected storage and transmission of confidential medical data; and (4) software which facilitates the review or implementation of clinical trial protocols; (5) software and hardware applicable to tying in data from multiple and simultaneous clinical protocols across multiple clinical sites; and 6) methods and instrumentation to support clinical imaging data.

G. Development of vectors for gene therapy, with improved means of: (1) targeting specific cells and/or tissues; (2) transduction and expression; (3) delivery to patients; and/or (4) production and purification.

H. Development of high throughput technologies for studies of human diseases and methods and techniques for the analyses, storage, and interpretation of accumulated data.

I. Development of techniques, instruments and reagents to optimize the recovery and quality of cells obtained from vertebrate and human organs for subsequent use in either basic research or clinical protocols.

J. Development of techniques, instruments, reagents and vector systems for use in clinical gene therapy protocols.

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Development of Discovery-Oriented Software and Tools for Science Education

Development of new discovery-oriented educational software and the application of educational technology and tools for education on health science topics that targets K through 12 students and undergraduate students are sought. Topics can range from basic molecular and cellular biology to human diseases. Development of this software may be directed toward the adaptation of existing or recently developed educational programs for interactive learning. This effort is intended to yield efficient and user-friendly educational units for K-12 and undergraduate students that can be extended to enhance the health science literacy of the general public. A broad dissemination is strongly encouraged.

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NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)

The mission of the National Center for Complementary and Alternative Medicine (NCCAM) is to explore complementary and alternative healing practices in the context of rigorous science; educate and train complementary and alternative medicine (CAM) researchers; and disseminate authoritative information to the public and professionals. CAM encompasses those healthcare and medical practices that are not currently an integral part of conventional medicine. The list of practices that are considered CAM changes continually as CAM practices and therapies that are proven safe and effective become accepted as "mainstream" healthcare practices. NCCAM groups these practices within four major domains of mind-body medicine (for example, meditation), biologically based practices (for example, herbal therapies, special diets), manipulative and body-based practices (for example, chiropractic, massage), and energy medicine (for example, Reiki, Qi gong). In addition, NCCAM also studies whole medical systems (for example, Traditional Chinese Medicine, Ayurveda). For a detailed description of NCCAM mission, please see http://nccam.nih.gov/about/plans/2005/index.htm.

The following narrative indicates the scope of projects suitable for the SBIR/STTR program that fit within the mission of NCCAM. For additional information about areas of interest to NCCAM and a listing of NCCAM's currently funded applications, please visit http://www.nccam.nih.gov/research. Business concerns interested in exploring SBIR/STTR grant opportunities with NCCAM are encouraged to contact the NCCAM representatives prior to submitting an application.

Technology Development and Research

NCCAM encourages innovative technological research and development of commercializable CAM products that would fulfill the mission of NCCAM. The application may include basic, pre-clinical, and early phase clinical studies that can ultimately lead to a commercial CAM product. The areas of interest to NCCAM include but are not limited to:

- Develop and validate methods for standardization and characterization of active ingredients in natural products;
- Develop and validate CAM methodology to enhance vaccine efficacy;
- Develop and validate methods for standardization and characterization of active components of mind-body interventions;
- Develop and validate devices for measurements of putative healing energies;
- Develop and validate biomarkers for measurement of stress for studying efficacy of mind-body therapies;
- Develop and validate standardized and reliable surrogate markers of brain states that correlate with brain imaging;
- Develop and validate technical imaging tools or instruments for studying manipulative therapies;
- Develop tools for pain management that are not conventionally accepted;
- Develop and validate unconventional devices for diagnosis and treatment; and
- Develop standardized, research-grade natural products including engineering of new probiotics. For biologically active agents, the applicant should pay particular attention to the NCCAM policy and guidance at http://nccam.nih.gov/research/policies/bioactive.htm.

Topics That Are of Little or No Interest to NCCAM

The NCCAM Office of Communications is responsible for disseminating CAM information to the public. Therefore, applications addressing database creation or maintenance of any kind, software development, or educational materials or courses (e.g., CD's, CME's) will not be considered relevant to the NCCAM SBIR/STTR program. Included are cookbooks of special diets and software or instructional materials for treatment of diseases. The NCCAM will also not support clinical practice of any kind.

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NATIONAL CENTER ON MINORITY HEALTH AND HEALTH DISPARITIES (NCMHD)

The mission of the National Center on Minority Health and Health Disparities (NCMHD) is to promote minority health and to lead, coordinate, support, and assess the National Institutes of Health (NIH) effort to reduce and ultimately eliminate health disparities. In this effort, the NCMHD conducts and supports basic, clinical, social and behavioral research, facilitates the development of research infrastructure and training, fosters emerging programs, and reaches out to racial/ethnic minority and other health disparity communities.

NCMHD particularly serves as the focal point for targeted, hypothesis-driven, patient-oriented research and targeted applied, outcomes- and problem-driven studies that meet at least two of three criteria: (1) participating health disparity population(s) is/are over sampled; (2) the participating health disparity population(s) is/are specifically targeted with or without within-group comparisons; and/or (3) the research focus is within the scope of NCMHD programmatic interests. NCMHD's programmatic interests include surveillance, explanatory, and translational research in health disparity populations. Specific topics include health promotion and disease prevention and intervention; pathogenic mechanisms underlying escalations in the susceptibility to disease and illness; and health services research - the impact of socioeconomic, cultural, and other environmental factors on health outcomes.

PROGRAM AREAS OF INTEREST

Natural History of Disparities in Health Outcomes

Disparities in health outcomes are believed to result from the interaction of a plethora of interactive factors such as environmental exposures and genetic traits, and/or the accrual over time of stable phenotypic traits and lifestyle behaviors that contribute to but are insufficient individually to cause the onset of disease or illness. The etiology of disparities in health outcomes with particular emphasis on identifying and deconstructing the array of interactive risk factors—environmental, socioeconomic, stereotyping, bias, clinical uncertainty, and gene-related factors—that contribute to escalations in the susceptibility to disease and illness and may contribute to health disparities. Examples include, but are not limited to:

1. Multidisciplinary basic research approaches that lead to biological probes and starting points for therapeutic interventions;
2. Innovative high throughput screening approaches to identify compounds that are active in target- and phenotype assays and to use these approaches to develop bioactive probes for application in vitro and potentially in vivo studies;
3. Methodological and technological innovation that will integrate behavioral and social science with biomedical research, including gene related and environmental components.
4. Differential pharmacologic drug metabolism; and
5. Impact of dietary decision making in diverse populations and effect on health disparity outcomes.

Health Promotion and Prevention Research in the Health Disparities Communities

High priority is given to activities designed to empower health disparity communities to achieve health equity through health education, disease prevention, and partnering in community-based hypothesis, outcomes- and problem-driven research.

Examples of such activities include, but are not limited to:

6. Efficacy of therapies in local populations;
7. Motivating positive behavioral changes in diverse populations;
8. Health outcomes related to health seeking, lifestyle, risk taking, protective behaviors and/or socioeconomic status;
9. Incorporating research into health promotion and disease prevention initiatives, applying new knowledge in a culturally appropriate manner in intervention/disease prevention initiatives; and
10. Distribution of health structures and adverse health effects, and the sufficiency of healthcare frameworks in accommodating diverse social, cultural, political and economic factors.

Innovations in Health Disparities Research

Studies that promote and advance evidence-based transformation in medical decision-making and health policy; demonstration projects that implement evidence-based, culturally sensitive intervention/disease prevention therapies and diagnostics; and activities designed to build capacity for health disparities research are of high priority. Examples of such studies include, but are not limited to:

11. Development of health disparity group-specific methodologies and diagnostics;
12. Development of technologies targeted for health disparity groups (i.e., gene chips, other novel assay systems, animal models, specialized instruments, etc.); and
13. Demonstration projects that build capacity for health disparities research (e.g., regional hospital-based registries for disease areas of emphasis, etc.) or implement the translation/application of research results in a culturally sensitive manner.

For additional information about the areas of interest to the NCMHD, please visit our home page at http://www.ncmhd.nih.gov.

Broad Area of Research that we Support

Studies on the biological and biobehavioral risk factors for disparities in health and health outcomes; cultural, environmental, and societal dimensions of disparities in health status, including the impact of health processes; development and refinement of research tools, survey instruments, and databases that are culturally sensitive and specifically for racial and ethnic minority populations and other health disparity populations, in particular the medically underserved which includes the rural and urban poor.

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NATIONAL LIBRARY OF MEDICINE (NLM)

The NLM supports research and development projects in biomedical informatics and bioinformatics. NLM defines biomedical informatics as the intersection of basic informational and computing sciences with a wide range of application domains in biomedicine and public health. Bioinformatics is the intersection of basic informational and computing sciences with the biological sciences.

For additional information about areas of interest to the NLM, please visit our home page at http://www.nlm.nih.gov/ep.

Biomedical Informatics

There are broad needs for informatics concepts, tools and systems to manage the information of health care delivery, reduce medical errors, provide decision support for clinicians, extract outcome and public health information from large datasets, and predict health events.

To support such projects, NLM is interested in:

A. Mechanisms to capture and integrate new information into existing knowledge bases, including integration of heterogeneous data sets.

B. Approaches for retrieving, extracting and analyzing data from large health-related and heterogeneous databases, such as patient data, population health data, or image databases.

C. Systems, devices, or programs that facilitate utilization of electronic medical record systems in clinical practice, for such functions as chart entry, decision support, reduction of errors.

D. Systems, devices, or programs that facilitate utilization of electronic record systems and tools in public health, for such functions as syndromic surveillance and trend analysis.

E. Projects relevant to the informatics of disaster management, including management and delivery of information in disaster settings.

Bioinformatics

High through-put scientific research has greatly increased the volume of research data and has magnified the problem of information management and interpretation.

To help manage such data, NLM is interested in:

A. Software algorithms and database query methods capable of capturing scientific data from published knowledge sources or multiple related factual databases.

B. Tools for data management and analysis for genetic linkage mapping, physical mapping, DNA sequencing, and proteomics.

C. Tools and systems for bringing "bench to bedside," applying research data to clinical problems.

D. Algorithms capable of predicting structure and/or function in model biological systems.

E. Algorithms capable of enhanced computational modeling of biological, biomedical and behavioral sciences data at multiple scales of research, ranging from molecular to population.

Other Research Topic(s) Within the Mission of NLM by pre-arrangement with NLM Program Staff

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CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

CDC will accept SBIR grant applications on the April 1, August 1, and December 1, 2006 submission dates.

The CDC serves as the national focus for developing and applying disease prevention and control, environmental health and health promotion and health education activities designed to improve the health of the people of the United States. To accomplish its mission, CDC identifies and defines preventable health problems and maintains active surveillance of diseases through epidemiologic and laboratory investigations and data collection, analysis, and distribution; serves as the PHS lead agency in developing and implementing operational research aimed at developing and testing effective disease prevention, control and health promotion programs; administers a national program to develop recommended occupational safety and health standards and to conduct research, training, and technical assistance to assure safe and healthful working conditions for every working person; develops and implements a program to sustain a strong national workforce in disease prevention and control; conducts a national program for improving the performance of clinical laboratories; and develops programs to prevent premature death and avoidable illness and disability

caused by noninfectious, non-occupational environmental and related factors.

CDC is responsible for controlling the induction and spread of infectious diseases, and provides consultation and assistance to other nations and international agencies to assist in improving their disease prevention and control, environmental health, and health promotion activities.

For additional information about areas of interest to the CDC, please visit our home page at http://www.cdc.gov.

NATIONAL CENTER ON BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES (NCBDDD)

The National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention seeks to promote optimal fetal, infant, and child development; prevent birth defects and childhood developmental disabilities; and enhance the quality of life and prevent secondary conditions among children, adolescents, and adults who are living with a disability.

The NCBDDD areas of interest focus on:

A. Develop, produce and evaluate the effectiveness of educational modules for birth defects prevention.

B. Develop, produce and evaluate the effectiveness of educational modules with the goal of preventing developmental disabilities.

C. Develop and evaluate assistive technology for promoting and maintaining health and reducing secondary conditions.

D. Develop and evaluate tools, modules or materials to identify children with developmental problems including developmental and early hearing screening.

Other Research Topic(s) Within the Mission of the Center

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NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)

The NCCDPHP plans, directs, and coordinates programs in health promotion, chronic disease prevention, and reproductive health to enhance quality of life, improve reproductive health, and reduce the incidence of heart disease, stroke, cancer, diabetes, arthritis, obesity, oral disease, infant and maternal morbidity and mortality, unintended pregnancy, and emerging chronic diseases. NCCDPHP uses two essential criteria to prioritize its research portfolio, societal burden and disproportionate burden. NCCDPHP places high priority on chronic diseases and conditions and reproductive health outcomes that have the greatest total impact on health, longevity, and quality of life. NCCDPHP places high priority on eliminating disproportionate burden related to sex, age, race, ethnicity, geography, sexual orientation, socioeconomic status, disability, and special needs. NCCDPHP supports three primary types of applied research, research on cause (determinant research), research on effect (intervention research), and research on application and benefit (dissemination

research). NCCDPHP emphasizes cross-cutting research that is participatory, accounts for social and ecological factors, and is implemented at multiple levels.

NCCDPHP has identified ten priority research areas: (1) develop new measures and research designs to strengthen the quality of research; (2) identify the underlying determinants of racial and ethnic health disparities; (3) develop and evaluate interventions to eliminate health disparities; (4) examine established and emerging risk factors for chronic disease and investigate their potential for public health interventions; (5) assess the effectiveness of policy and environmental interventions to promote health; (6) improve the processes and outcomes of health care systems; (7) develop effective communication strategies to promote health; (8) examine methods for helping people manage their own health; (9) develop and evaluate the effectiveness of population-based health promotion and disease prevention policies and programs at the local, state, national, and international levels; (10) examine approaches for effectively translating successful community interventions into widespread practice. For examples of specific research questions in each of the ten priority areas, see *Setting the Agenda: CDC Research in Chronic Disease Prevention and Health Promotion*, available at http://www.cdc.gov/nccdphp/agenda/index.htm.

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Division of Cancer Prevention and Control

The National Center for Chronic Disease Prevention and Health Promotion supports a national program to prevent premature death and disability from chronic diseases and to promote healthy personal behaviors. Within the Center, the Division of Cancer Prevention and Control supports comprehensive cancer surveillance, epidemiologic, health and behavioral science research, communications and program services to reduce the illness and death associated with cancer.

Division of Cancer Prevention

The Cancer Surveillance Branch of the Division of Cancer Prevention and Control supports Cancer Registration activities in population based cancer registries. This national program with its partners encompasses the entire research, evaluation, collection, and analysis phases of cancer surveillance data for use in comprehensive cancer control plans.

A. Promote the advancement and utilization of real-time standardized computerized interfacing from Hospital Registry systems to medical record data sources and to Population based cancer surveillance systems. Activities would include improve the communication and computerized interface technology such as the establishment of Virtual Private Network, and secure Internet technologies to facilitate the secure reporting of data from providing organizations; innovations and application of mapping of local codes to national clinically relevant standard codes (such as LOINC and SNOMED) and vice-versa; advancement in the use of standardized reporting structures such as Health Level 7 (HL7) standards and Extensible Markup Language (XML).

B. Develop innovative presentation of cancer research and surveillance data such as graphical information systems for the analysis of data, and improved innovation in the design and use of management reports.

C. Promote the advancement and development of integrated person centered data repository with other appropriate data systems applying cancer registry data and other disease registries and vital records data.

D. Develop innovative and automated computerized data quality improvements, such as the application of intelligent business rules for use in cancer registry applications. Such that when modification are adjusted to a patients cancer abstract all necessary modifications are done based on appropriate automatic quality control checks.

E. Promote the development of probabilistic matching models for auto-encoding of narrative text based medical records sources such as narrative pathology, endoscopy, or surgery reports to standardized reporting codes.

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Breast Cancer Early Detection

The Breast and Cervical Cancer Early Detection Program in the Division of Cancer Prevention and Control is a national program to coordinate and improve the delivery of comprehensive breast and cervical cancer screening and diagnostic services to low income women who lack the income or insurance coverage necessary to participate in these potentially lifesaving procedures, with an emphasis on reaching women from minority populations who are less likely to have access to or participate in them. Breast cancer screening is directed to women age 40 and older. Women diagnosed with breast cancer are most likely to survive when their disease is detected at a very early stage.

Early detection is primarily a function of routine mammography and expert interpretation. In the U.S., a clinical breast examination (CBE) is considered part of the screening process. Clinical breast examination can provide useful information to the radiologic technician and the mammographer concerning areas of the breast that should receive special attention in imaging, or conditions that may suggest alternate techniques of imaging. Practitioners being trained to do CBE frequently use synthetic breast models to simulate examinations. These models are typically representative of relatively dense breasts, and they are modest in size. Opportunities exist to improve the skills of clinicians in examining breasts by making available a wider variety of models that reflect both larger breasts and tissue more typical of post-menopausal women.

Applicants would propose a plan to identify existing models, document gaps, and create models to fill those gaps. Phase two of the proposal would present a plan to market/disseminate the models and evaluate their impact on the practice of CBE.

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Division of Adult and Community Health

The mission of the Division of Adult and Community Health, NCCDPHP, has seven major components:

1. ***Aging.*** CDC has established national, state-based programs targeting cardiovascular disease, diabetes, cancer, arthritis, injuries, and immunization. CDC's unique expertise can be readily applied to target the health needs of older Americans by providing public health leadership and coordination, by enhancing surveillance, and by putting research to work for older Americans.
2. ***BRFSS.*** The Behavioral Risk Factor Surveillance System (BRFSS), the world's largest on-going telephone survey, tracks health and behavioral risk factors in the United States, including all 50 states, the District of Columbia, Puerto Rico, Guam, and the Virgin Islands. BRFSS is one of the leading innovators of survey research methods and approaches, including the uses of mixed-mode surveys, addressing changes in telecommunications technology such as cell phones, and surveying hard-to-reach racial and ethnic groups.
3. ***Cardiovascular Health.*** Heart disease and stroke are the first and third leading killers of Americans and are leading causes of disability in the US. Cardiovascular diseases cost an estimated $368 billion in 2003. High blood pressure and high blood cholesterol, major risk factors for heart diseases and stroke, are prevalent in the US population yet are preventable and controllable. CDC's cardiovascular health program mission is to provide public health leadership to improve cardiovascular health for all, reduce the burden, and eliminate disparities associated with heart disease and stroke.
4. ***Health-Related Quality of Life Surveillance.*** In public health and medicine, the concept of health-related quality of life refers to a person's or group's perceived physical and mental health over time. Tracking health-related quality of life

in different populations can identify subgroups with poor physical or mental health and can help guide policies or interventions to improve their health.

5. ***Prevention Research Centers.*** The PRC Program is a network of academic centers, public health agencies, nonprofit organizations, and community partners that strives to improve health promotion and disease prevention efforts. The centers, which focus on high-priority public health issues, work to bridge gaps between scientific knowledge and public health practice. The network translates promising research findings into practical and effective programs and policies for use in communities throughout the nation.

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Division of Nutrition and Physical Activity

The Division of Nutrition and Physical Activity is partnering with the National Cancer Institute (NCI), the Produce for Better Health Foundation (PBH), the United States Department of Agriculture (USDA), the American Cancer Society (ACS), and others on the 5 A Day for Better Health Program, an initiative to increase American's intake of fruit and vegetables. High intake of fruit and vegetables has been associated with reduced risk of cardiovascular disease, many cancers, as well as other chronic diseases and conditions. Further, over consumption of food combined with lack of physical activity is creating an epidemic of overweight and obesity in the United States. Opportunities exist to prevent or reduce the burden of many chronic diseases by increasing knowledge of nutrition, increasing availability of and access to healthy foods, and changing policies to promote healthful choices.

Chronic Disease Nutrition

There is interest in the development, dissemination, and evaluation of innovative methods to increase knowledge of healthful nutrition practices including increased fruit and vegetable intake, decreased fat intake, and decreased caloric consumption among persons of many different backgrounds and at different stages of life. Although effective strategies for nutrition education exist, few have been disseminated to a larger audience than the original research population. The focus of proposed projects should reflect target populations at high risk of developing nutrition related chronic diseases. There is also interest in the development of nutrition intervention programs that are targeted toward changing the environment or policies that affect people's food choices. Most nutrition interventions provide nutrition education for individual dietary change but do not change the environment or policies that affect a population's access to healthful foods. Some limited research has examined how the availability of and access to fruit and vegetables impacts consumption. Environmental and policy interventions to increase availability and reduce prices of fruit and vegetables have been effective in the short-term. Few of the interventions have lasted long enough to determine whether increased consumption could be sustained over the long-term.

A. Use of innovative or new strategies to promote health.

1. Design and develop an innovative series of educational tools (i.e. audiovisuals, series of lunch and learns) for a worksite health promotion program that incorporates both the volumetrics/energy density principles as well as the promotion of fruits and vegetables. The educational series should clearly define the benefits of eating fruits and vegetables and explain the volumetrics/energy density eating concept. In addition, it should be emphasized that replacing high-energy dense foods for low-energy dense foods can help a person eat fewer calories. Some examples of educational tools include a video on shopping for and preparing food; a video on the principles of Volumetrics with specific examples of varying levels of energy density in foods; a supermarket tour guide (with an emphasis on fruits and vegetables); a video or booklet on how recipes can be modified to incorporate fruits, vegetables and low-energy dense foods; as series of lunch and learns with handouts. A successful intervention should target the specific population – working adults who have little time to think about, prepare and cook meals. In addition, the tools should reach different ethnic and socioeconomic groups. This program

should be supported at work but also translatable into the employee's everyday life both at home and away from home. Coordination on this project with CDC's 5 A Day Program is strongly encouraged for a successful outcome.

2. Design, develop, and evaluate methods to encourage purchase of simple, time saving, fresh, and good tasting healthful food items in supermarkets, convenience stores, or other locations. Some examples of supermarket methods include dinner of the day (i.e., a rack that conveniently contains all items needed for a healthy meal including recipe information), convenience meals, or healthy children's lunch packs. Some examples of convenience store methods include a rack at the front counter containing individually wrapped snack packs or items packaged to be eaten on the go (e.g., a fruit cup with spoon that can fit in an automobile drink holder). Coordination on this project with CDC's 5 A Day Program is strongly encouraged for a successful outcome.

3. Design, develop, and evaluate innovative food service alternatives for use at schools, colleges, workplaces, or other locations. Some examples include smoothie bars, mobile salad bars, burrito or pasta bars, vending machine alternatives, or other similar options. Several of these food service alternatives have been tried in school systems and worksites across the country. This program should incorporate and promote increased consumption of fruits and vegetables. Examples to follow include the Santa Monica Farmer's Market Salad Bar Program, innovative changes in food service in the Los Angeles County School System, Chefs in schools and successful research interventions that changed availability and pricing in school or workplace cafeterias and vending machines. Coordination on this project with CDC's 5 A Day Program is strongly encouraged for a successful outcome.

4. Design, develop, and evaluate (pilot test) a comprehensive educational strategy/program with school aged children and young adults (preschool to college) that focuses on increased vegetable and fruit consumption. This comprehensive educational strategy/program may be school or community based. It should be interdisciplinary, have a multi-dimensional approach, be theory based and generalizable. Partnering is encouraged with those entities interested in improving community health. Innovations may include interventions in other youth organizations or programs such as Boy and Girl Scouts, 4-H Boys and Girls Clubs, YMCA, and college groups. Coordination on this project with CDC's 5 A Day Program is strongly encouraged for a successful outcome.

5. Environmental change interventions can be an effective way to support a community effort to increase community vegetable and fruit intake. Design, implement, and evaluate an environmental change intervention incorporating 5 A Day. This intervention should be an educational and ecological effort emphasizing such factors as access to vegetables and fruits, cost/pricing of vegetables and fruits, and point-of-purchase education. Behavior-specific ecological models should be used to guide this intervention. This intervention may use innovative methodology and partnering to facilitate consumption of vegetables and fruits (examples include: strategies for edible trails, Jr. Master Gardener projects, (Senior) farmers markets and/or school and community gardens).

6. Design, develop and evaluate a prototype 5 A Day program that addresses the motivational factors influencing American adolescent decision making in terms of nutrition-related behaviors. The 5 A Day message is clearly not getting through to America's adolescents. Most 5 A Day programs seem to target either children or adults, with little attention paid to the teenager. Informational websites are either loaded with dry facts aimed at adults, or contain child-oriented themes, using animated fruit and vegetable characters, very simple games, or novelty songs to entice children to change their dietary habits. What about all the adolescents who have already developed poor dietary habits and perceptions? This program should address/ determine specifically how adolescent *nutrition-related* perceptions are formed, what it takes to change these perceptions, how adolescents view existing

nutritional programs (and nutrition in general), and most importantly, how to create a positive change in adolescent dietary habits. Coordination on this project with CDC's 5 A Day Program is strongly encouraged for a successful outcome.

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Physical Activity and Health

Regular physical activity has a positive impact on numerous health outcomes. As such, the accurate measurement of individual physical activity behaviors is important for both surveillance and research.

Applications are invited for the development of innovative technological strategies and methods for improving the validity and reliability of self-reported physical activity behaviors. Of interest is the development and validation of technological tools that will allow qualification of the CDC/ACSM physical activity recommendations of individual behaviors. The product should improve upon current survey or diary methods as they relate to: a) the recall and reporting of specific activities, frequency, intensity, duration and/or b) respondent burden. Examples of technological tools could include, but are not limited to, software for hand-held electronic devices for individually-tailored survey assessment, software for assessment that is aided by video examples of physical activity behaviors, and software for improved physical activity diaries. Development of such tools will allow for better measurement of physical activity for surveillance and research.

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Division of Oral Health

The Division of Oral Health seeks to improve the oral health of the nation by extending the use of proven strategies to prevent oral diseases, enhancing surveillance of oral diseases, strengthening the nation's oral health infrastructure, and guiding infection control in dentistry. At the core of the DOH mission is the critical relationship between oral health and general health and well-being. Division programs focus on educating the public, public health and clinical professionals, and policy makers on steps that individuals and communities can take to improve oral health at different ages throughout the lifespan, and serving as a resource for these efforts.

A. Providing Safe Dental Care

Infection control in the dental care environment remains essential to ensuring the public's safety and retaining its confidence. In the 15 years since CDC published its first guidelines for infection control in dentistry, infection control practices have dramatically improved. Nevertheless, the potential for disease transmission during visits to the dentist continues to arouse intense public interest and media scrutiny. To minimize this potential, CDC assesses the risks of infectious disease transmission, updates guidelines to minimize those risks, investigates disease outbreaks and environmental hazards in dental settings, and identifies emerging problems. Infection control activities address the "Healthy People 2010" priority areas in Occupational Safety and Health, Immunization and Infectious Diseases, and HIV Infection.

1. Develop surveillance system(s) and outcome measures for adverse events related to exposure to pathogens and other hazardous agents during dental treatment.
2. Develop methods or models for evaluating the effectiveness and cost-effectiveness of infection control interventions.
3. Develop dental devices with passive safety features that meet or exceed performance criteria identified by CDC (www.cdc.gov/oralhealth/infectioncontrol/forms.htm).
4. Develop devices, both accurate and passive, to measure biofilm or bacterial contamination in dental waterlines.

5. Develop educational/training materials and demonstrate their effectiveness in on-the-job training of dental assistants in dental office infection control and quality assurance.
6. Develop training and educational materials for using the oral rapid HIV screening test in dental facilities to identify cases of HIV infection that may otherwise go undetected.

B. Oral Health

In collaboration with several partners, the Division develops national plans and supports programs in specific areas of oral health including appropriate use of fluorides and sealants to prevent dental caries (tooth decay); activities that address the oral health needs of an aging population; and implementation of strategies to reduce disparities in oral health status. This includes expanding the capacity and ability of state health departments to implement community water fluoridation and school-based/-linked dental sealant programs. The following are topics of interest in oral health.

1. Develop accurate, non-invasive methods or devices to aid in diagnosis, measurement, and recording of dental caries.
2. Identify biomarkers or develop methods or devices to measure total fluoride exposure.
3. Develop oral hygiene products or devices for adults with motor difficulties.
4. Develop innovative fluoride delivery systems for home use among persons at increased risk for dental caries (tooth decay).
5. Develop innovative methods to defluoridate water with high natural fluoride concentrations.
6. Develop innovative sealant materials, supplies or equipment for use by sealant programs in non-traditional dental settings.

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Division of Reproductive Health

Mission

The mission of the Division of Reproductive Health (DRH) is to promote optimal reproductive and infant health and quality of life by influencing public policy, health care practice, community practices, and individual behaviors through scientific and programmatic expertise, leadership, and support.

The Division accomplishes its mission by working with partners throughout the nation and world to

- Conduct epidemiologic, behavioral, demographic, and health services research.
- Support national and state-based surveillance systems to monitor trends and investigate health issues.
- Support scientific and programmatic development within states and other jurisdictions.
- Provide technical assistance, consultation, and training worldwide.
- Translate research findings into health care practice, public health policy, and health promotion strategies.

Goals

- **Outcomes** – Improve and promote infant health and reproductive health, and well being of men and women globally.

- **Leadership** – Provide global leadership to optimize reproductive and infant health.
- **Research** – Define, conduct, and promote public health research in reproductive and infant health.
- **Translation** – Translate science and technology into strategies and interventions that promote reproductive and infant health.
- **Infrastructure** – Maintain a healthy, productive environment, which supports achievement of the mission.
- **Capacity Building** – Enhance the ability of others to identify and address reproductive and infant health issues.

Priorities

- Women's Reproductive Health
- Unintended Pregnancy Prevention
- Maternal Health
- Infant Health
- Global Reproductive Health

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NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

The National Center for Injury Prevention and Control plans, directs, and coordinates a national program to maintain and improve the health of the American people by preventing premature death and disability and reducing human suffering and medical costs caused by nonoccupational injury, addressing both intentional injuries that result from violent and abusive behavior and unintentional injuries. The national program encompasses the prevention of nonoccupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons. The Center will address injury prevention and control through an orderly sequence of activities beginning with research on causes, circumstances, and risk factors; progressing through research on interventions and their impact on defined populations. These activities then lead to the broad, systematic applications of interventions that are soundly based scientifically.

CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. CDC encourages applicants to submit grant applications with relevance to the specific objectives of this initiative. Potential applicants may obtain a copy of "Healthy People 2010"; (Full Report: Stock No. 017-001-00537-1): through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325, (202) 512-1800.

More recently, the Centers for Disease Control has published its *CDC Injury Research Agenda*, June 2002, Atlanta Georgia, which identifies 95 research themes in various areas of injury research, including preventing injuries at home and in the community and in sports, recreation and exercise, preventing transportation injuries, preventing intimate partner violence, sexual violence, child maltreatment, youth violence and suicidal behavior and acute care, disability and rehabilitation. The full report is available at http://www.cdc.gov/ncipc.

The focus of the research topics for SBIR should reflect the themes represented in the research agenda designed to control injury morbidity, mortality, disability, and costs. These projects may be categorized by the three phases of injury prevention and control. Research topics of interest include, but are not limited to:

A. ***Prevention.*** There is interest in the development, application, and evaluation of innovative interventions applicable to intentional and unintentional injury. The focus should reflect target populations at high risk for injury and injury consequences, including minorities, children, the elderly, rural residents, and farm families. SBIR projects that have relevance for reducing injury or increasing dissemination and adoption of effective injury prevention interventions are sought. The following are examples:

1. Develop technology to improve technology transfer on effective interventions to prevent unintentional injuries and violence.
2. Develop a practical, valid tool to measure the adequacy of supervisory practices to prevent childhood injuries, such as drownings and falls.
3. Develop technology-based methods to obtain exposure and injury incidence data for injuries in sports and recreational activities.
4. Develop new improved and practical alcohol breath testing devices that can be used in multiple settings (by enforcement personnel, bar patrons, and the public).
5. Develop environmental and behaviorial devices that can assist in the prevention of pedestrian injuries, including technology-based strategies that provide feedback to drivers and walkers about impending hazards.
6. Design, develop, and evaluate educational materials to train public health personnel in injury prevention that could be adapted for medicine, nursing and allied health.
7. Develop and evaluate injury and violence prevention materials uniquely targeted to and disseminated in medical care and managed care settings, such as in-house kiosks, computer-based self-assessments, and clinical preventive services based interventions or through the use of distance-based learning technology. These materials can address topics such as falls, helmets, supervision and prevention of youth violence or intimate partner violence.
8. Develop and test a passive alcohol sensor device to passively measure the blood alcohol level of injured patients arriving at the emergency department.
9. Develop products to improve monitoring and control of exposure to violent media.
10. Develop innovative educational products to teach non violent resolution of conflicts in partner or family situations.
11. Develop and evaluate video/computer technology to improve staff training and program fidelity monitoring of efficacious parent training programs for the prevention of child maltreatment.

B. ***Acute Care.***

1. Develop developmentally appropriate devices, instruments, methods, models, tests, and computer software related to the full spectrum of acute care of the trauma patient, beginning with the establishment of access to emergency care, response at the injury scene, transportation of the critically injury, to management of postoperative complications such as multiple organ failure syndrome.
2. There is a need to improve diagnostic modalities in several areas, particularly in those related to perfusion and oxygenation at the tissue level. Further, among those patients whose bleeding has been controlled and who will survive the acute phase of injury, the major causes of death are irreversible cerebral damage or uncontrollable cerebral swelling and multiple organ failure. There is an urgent need for research into methods of reducing secondary cerebral injury and of controlling brain swelling and preventing multiple organ failure.
3. Design, develop and evaluate Emergency Department-based prevention services for the identification and referral of persons at risk for violence or alcohol-related injury.

C. ***Rehabilitation.***

1. Develop developmentally appropriate adaptive equipment, assistive devices, and

instructional materials directed toward preventing or minimizing the secondary complications of individuals with traumatic brain or spinal cord injuries including cognitive learning problems, pressure ulcers, contractures, muscular atrophy, skeletal deformity and other definable conditions.

2. Design, develop and evaluate educational materials for persons with traumatic brain or traumatic spinal cord injury, their families and/or caregivers that are directed toward preventing or minimizing the secondary complications associated with these injuries.
3. Develop training materials to assist persons with disabilities and their care givers to safely and efficiently evacuate various buildings, (e.g., multi-storied structures) in emergencies.
4. Develop products to improve monitoring and control of exposure to violent media.
5. Develop innovative educational products to teach non violent resolution of conflicts in partner or family situations.

Other Research Topic(s) Within the Mission of the Center

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NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)

The NIOSH plans, directs and coordinates the national program effort to develop and establish recommended occupational safety and health standards and to conduct research, training, and related activities to assure safe and healthful working conditions for every working man and woman. NIOSH has both a regular grant program and an SBIR grant program; the purpose of both is to develop knowledge that can be used in preventing occupational diseases and injuries. In the regular NIOSH grant program, the following types of applied research projects are supported: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational diseases and injuries; methods research to develop more sensitive means of evaluating hazards at work sites, as well as methods for measuring early markers of adverse health effects and injuries; control research to develop new protective equipment, engineering control technology, and work practices to reduce the risks of occupational hazards; and demonstrations to evaluate the technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system.

Control Technology and Personal Protective Equipment

Engineering controls, administrative policies, and personal protective equipment are needed to manage exposures to occupational hazards. Engineering controls include substitution of a safe material for a hazardous one, design changes to equipment, or modification of work methods to eliminate or reduce hazards. Changes in work practices and management policies and training programs are examples of administrative controls. In some cases where it is not otherwise possible to maintain a healthy work environment, personal protective equipment such as respirators and protective clothing can be used to isolate workers from the hazard. Research is needed to develop and evaluate control strategies for specific hazards and

to assure their practicality and usability in workplaces.

A. Improve the effectiveness of existing or proposed engineering controls (including retrofit solutions).

B. Develop control measures for new workplace hazards.

C. Develop products or approaches that reduce/eliminate the specific hazardous parts of a job that contribute most to the actual exposure, including personal hygiene where contamination of surfaces, clothing, or skin may occur.

D. Develop personal protective equipment that will fit the anthropometric diversity in today's workforce.

F. Develop alternatives to pesticide application and hazardous waste remediation.

G. Develop micro sensing devices to notify workers before chemicals break through protective clothing and identify failures in containment systems for hazardous materials.

H. Develop new materials for clothing to protect against chemical and physical hazards.

I. Develop information dissemination methods to help businesses learn about and implement occupational safety and health programs.

J. Develop training materials to teach hazards and risks, demonstrate solutions, measure changes in behavior and practices, and improve injury and illness rates.

Exposure Assessment Methods

Exposure assessment is a multi-disciplinary field central to deciding whether and how to use resources for reducing workplace exposures, and to defining exposure-response relationships in epidemiologic studies. Rapid, inexpensive measurement tools and improved data analysis methods are needed for the collection of adequate exposure data and for effective intervention. At least three major gaps in current methods will drive development of exposure assessment methods in the next decade: (1) the lack of sufficiently precise exposure assessments to support accurate epidemiologic studies in the complex environments of today's workplaces, (2) the lack of practical measurement techniques that can be applied at reasonable cost in many workplaces where hazards may exist, and (3) the lack of validated methods for measuring relevant exposure and total dose data directly from biological samples obtained by relatively noninvasive techniques.

A. Develop computer models to extrapolate information from historical data of limited exposure measurements to apply to large study populations, and to incorporate short-duration but high-intensity exposures such as leaks or spills into the models.

B. Develop easy-to-use, direct-reading instruments and test kits to measure exposures rapidly and inexpensively in a variety of workplaces for routine monitoring, evaluating the success of control technologies, and providing data for research studies.

C. Improve the measurement of low concentrations of chemicals and biomarkers in biological specimens such as blood, urine, saliva and sweat so that such concentrations can be linked to internal dose at the target organs.

D. Design laboratory analytical methods for inexpensively measuring numerous chemicals in a single sample.

E. Formulate exposure survey designs and methods for exposure data analysis to obtain more meaningful data for health risk assessments.

F. Improve exposure assessment methods so that at-risk workers can be identified.

Intervention Effectiveness Research

The goal of intervention research is to develop practical strategies and techniques that effectively reduce or prevent workplace injuries and illnesses. Workplace safety and health interventions include but are not limited to developing and implementing specific engineering control technologies, process and work organization changes, information dissemination and health communication practices, worker/management participatory safety and health programs, safety and health training, selective use of personal protective equipment, and inspection and enforcement of protective exposure limits. Intervention research involves the testing and evaluation of interventions, programs, and policies. Although many intervention strategies have been applied to industrial settings, knowledge about what works best is limited. Corporate safety and health programs, regulatory requirements and voluntary consensus standards, workers' compensation policies and loss-control programs, engineering controls, and educational campaigns are among the

types of interventions that need to be developed, implemented, and evaluated.

A. Develop techniques to evaluate the effectiveness of implemented control technologies.

B. Develop materials and methods for increasing the acceptance of new control technologies and develop approaches to eliminate or alter these barriers, including economic feasibility.

C. Develop intervention efforts in the areas of greatest need.

Surveillance Research Methods

Surveillance systems describe where occupational hazards, injuries, or illnesses are found, how frequently they are found, whether they are increasing or decreasing, and whether prevention efforts have been effective. The public health community relies on surveillance information to set research and prevention priorities, but critical gaps in current systems limit their usefulness. These systems need to be updated and expanded, and new systems and methodologies need to be developed.

A. Develop approaches for implementing comprehensive, integrated national systems utilizing data sources and models of surveillance that exist in the public and private sectors.

B. Formulate methods to assess nationally or locally the impact of intervention efforts on worker safety and health.

C. As restructuring of health care delivery systems occurs throughout the United States, develop linkages among the systems to identify, track, and target occupational safety and health problems and provide information for decisions to develop interventions or to improve related medical care.

D. Investigate hazard surveillance systems as a means of identifying risks and exposures at worksites and industries, including risks associated with prototypes of new technologies, before injuries and illnesses occur.

Other Research Topic(s) Within the Mission of the Institute

Because of the diverse nature of occupational safety and health issues, many other research topics are supported by NIOSH in addition to the NORA topics. In addition, NIOSH supports research to reduce occupational injuries and illness in sector specific areas including construction, agriculture, and mining. Visit the NIOSH homepage for more information on NIOSH's research program areas http://www.cdc.gov/niosh/homepage.html.

Construction

Each day, construction workers face trench cave-ins, falls, machinery accidents, electrocutions, and motor vehicle incidents. NIOSH researchers identify causes of and develop programs to prevent injuries and fatalities in construction.

A. Commercialization of new designs or controls to reduce dust emissions from tools such as jackhammers.

B. Development of improved tool designs to reduce various hazards such as noise, vibration, or awkward postures.

C. Information tools to facilitate hazard recognition (e.g. for scaffolds, cranes, excavations) on job sites.

Agriculture

Agriculture ranks among the most hazardous industries. Farmers are at high risk for fatal and nonfatal injuries, work-related lung diseases, noise-induced hearing loss, skin diseases, and certain cancers associated with chemical use and prolonged sun exposure. Farming is one of the few industries in which the families (who often share the work and live on the premises) are also at risk for injuries, illness, and death.

A. Develop and evaluate devices that improve ladder safety.

B. Design and test improved safety and health training modules for Latino farmers.

C. Safe use of pesticides for limited English speaking and other minority farmers.

D. Roll over protection devices and roll over warning systems for older tractors.

Mining

The mining industry is one of the more challenging occupational sectors having to deal with adverse natural conditions such as cramped work space, poor visibility, handling of large volumes of bulky and heavy materials, and in many cases, a variety of unknowns including the physical characteristics of the materials being mined and the surrounding

materials with little knowledge of the conditions ahead of mining and difficulties in predicting and measuring the environmental conditions of the mine workings. These environmental conditions include dust concentrations, gas concentrations, noise levels, diesel particulate matter levels and noise levels. Advancements in technology and knowledge which would address any of the above concerns would be beneficial to improving worker health and safety in the mining industry. The advancements could be achieved through the development of new and innovation technologies, enhanced understanding of the conditions and improved approaches and strategies for dealing with the issues.

A. Develop new approaches for measurement or identification of conditions in the vicinity surrounding current underground mining operations.

B. Develop technology that has application for measuring or predicting the exposure of mine workers to any of the factors present in surface and underground mines. The factors include noise levels, diesel particulate matter and dust concentrations.

C. Determine the effectiveness of and/or develop improved approaches for training used to protect the health and safety of mine works.

D. Determine a methodology for evaluating the safety culture of the mining community and develop an improved model which enhances the overall safety of surface and underground mining operations.

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FOOD AND DRUG ADMINISTRATION (FDA)

FDA will accept SBIR grant applications on the April 1, August 1, and December 1, 2006 submission dates.

The mission of the Food and Drug Administration (FDA) is to protect the public health of the Nation as it may be impaired by foods, drugs, biological products, cosmetics, medical devices, ionizing and non-ionizing radiation-emitting products and substances, poisons, pesticides, and food additives. FDA's regulatory functions are geared to insure that foods are safe, pure, and wholesome; drugs, medical devices, and biological products are safe and effective; cosmetics are harmless; all of the above are honestly and informatively packaged; and that exposure to potentially injurious radiation is minimized.

For additional information about areas of interest to the FDA, please visit our home page at http://www.fda.gov.

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)

CBER is responsible for ensuring the safety, efficacy, potency and purity of biological and related products intended for use in the treatment, prevention or cure of diseases in humans as well as the safety of the nation's supply of blood and blood products. The primary responsibility of CBER is to review the quality, safety and efficacy of vaccines, blood products, certain diagnostic products and other biological and biotechnology-derived human products.

CBER's activities include: evaluating the quality, safety and effectiveness of biological products before marketing, and monitoring the pre-clinical and clinical testing of new biological products; licensing biological products and manufacturing establishments, including plasmapheresis centers, blood banks, vaccine and biotechnology manufacturers; AIDS program and policy activities, including research on AIDS therapeutic products, diagnostic tests and vaccines; research to establish product standards, develop improved testing methods and assess the safety of biological products; compliance, lot release program and post market surveillance; meeting PDUFA goals, new research programs, and new regulatory initiatives (managed review process for all products).

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

CDER develops FDA policy with regard to the safety, effectiveness, and labeling of all drugs for human use; evaluates new drug applications and investigational new drug applications; develops standards for the safety and effectiveness of all over-the-counter drugs; monitors the quality of marketed drugs through product testing (bioavailability/bioequivalence testing), post marketing surveillance, and compliance programs; develops guidelines on good manufacturing practices; conducts research and develops scientific standards on composition, quality, safety, and efficacy of human drugs.

Drug regulatory research as conducted in CDER is directed at the discovery of new knowledge relevant to drug development, postmarketing drug experience (patterns of drug use and safety), and drug regulation to enhance FDA regulatory decisions. These drug regulatory decisions impact on the development of regulations, guidelines and guidance for the regulated industry and provide clarity and consistency in application of CDER regulatory requirements. These drug regulatory decisions also impact public health by ensuring that marketing drugs are safe and efficacious and that their risk: benefit profile remains acceptable during the market life of a drug. Specific areas of research conducted by the Center include: Pharmacology/toxicology, microbiology/virology, clinical pharmacology, pediatric issues in drug therapy, postmarketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., datamining techniques), epidemiologic studies of therapeutics using population-based data, regulatory compliance, product quality, and active surveillance methods.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Develop a system for gathering real-time data on physician prescribing behavior, understanding and compliance with drug product labeling and frequency of off-label prescribing.

B. Develop and evaluate the effectiveness of new methods and tools for managing the known risks of marketed drug products (e.g., communicating newly identified risks to health care practioners and patients).

C. Develop methods for timely active surveillance of newly approved drug products in large populations to identify both expected and unexpected outcomes.

D. Develop methods for actively collecting information on all cases of classically drug-associated events (e.g., acute liver failure, blood dyscrasias, severe desquamating skin disorders) to augment the FDA’s current passive surveillance system.

E. Develop improved clinical markers and methods with potential for bed-side application for detection of the early onset of adverse drug events.

F. Develop surrogate potency methods for biotech drug products to replace traditional animal testing.

G. Development of psychochemical and in-vitro biological tests to evaluate pharmaceutical equivalence of complex drug substances and drug products.

H. Research into approaches to handle informative missing patient data in clinical trials, including innovations in study designs and statistical methods of analysis.

I. Statistical and computational methods and strategies for the design, analysis and interpretation of microarray, genomic and proteonomic data.

CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN)

The Center for Food Safety and Applied Nutrition conducts research and develops standards on the composition, quality, nutrition, and safety of food, food additives, colors, and cosmetics. The Center also evaluates FDA's surveillance and compliance programs relating to foods, colors, and cosmetics; reviews industry petitions and develops regulations for food standards to permit the safe use of color additives and food additives; collects and interprets data on nutrition, food additives, and environmental factors affecting the total chemical result posed by food additives; and maintains a nutritional data bank.

CFSAN regulates all foods **except** meat, poultry and processed egg products. CFSAN seeks research designed to complement and accelerate efforts for the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics.

The priorities of FDA's food defense research program are based on determining the food/agent combinations of highest concern. Mission-critical knowledge gaps are addressed through translational research concerning the need to anticipate, prevent, detect, respond, and recover from terrorists' assaults on the food supply. This requires research activities in five areas: (1) knowledge of the behavior of microbiological, chemical, radiological, and biologically-derived toxic agents in priority vulnerable foods during the stages of production, distribution, marketing, and preparation; (2) enhanced information on the susceptibility of the population to microbiological, chemical, radiological, and biologically-derived toxic agents via priority vulnerable foods; (3) identification and/or development of new techniques for "shielding" priority vulnerable foods through the development of new prevention and/or security technologies; (4) development of enhanced sampling and detection methods for priority agents in vulnerable foods including field deployable and in-line sensor-based screening, analytical, and investigational (forensic) technologies; and (5) development of effective methods for ensuring that critical food production and manufacturing infrastructure can be rapidly and effectively decontaminated in event of a terrorist attack. In accord with section 3402(d) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, FDA's food defense research is particularly focused on tests and sampling methodologies to detect intentional adulteration and tests that are suitable for inspections of food at ports of entry to the U.S. The mission-critical needs require that the research not stop at the generation of new knowledge and technologies, but also include the validation of those approaches under realistic conditions that reflect the diversity of the food industry, and the transfer of that technology to the appropriate sectors of the food industry.

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)

CDRH develops FDA policy and solves problems related to public health and safety of medical devices and radiation-emitting electronic products. It evaluates applications for premarket approval of medical devices, approves products development protocols and exemption requests for investigational devices. It classifies devices into regulatory categories, develops safety and effectiveness standards and good manufacturing practices regulations, operates postmarket surveillance and compliance programs, and provides technical, non-financial assistance to small manufacturers. The Center also conducts programs to reduce human exposure to hazardous ionizing and nonionizing radiation, through an electronic product radiation control program and other programs designed to control and to limit radiation exposure. The Center develops and conducts research and testing programs in the areas of physical, life, and engineering sciences related to the human health effects of radiation and medical device technologies, provides expertise and analyses for health-risk assessments, and also develops new or improved measurement methods, techniques, instruments and analytical procedures for evaluating product performance and reliability. The overall research program may be categorized into four areas, as follows:

1. Characterization of the constituents or components of products.
2. Measurement of product performance.
3. Bioeffects that derive from human exposure to radiation or medical devices.
4. Radiation metrology in support of Agency regulation of radiation-emitting products.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Develop an optical non-destructive method for rapid microtopographic evaluation and measurement of wear of articulating surfaces of implant prostheses.

B. Develop a system, including CDROM database of human chemical physiological, electrical and mechanical service environment test parameters, for use to design test protocols for implant device performance and for accelerated reliability testing.

C. Develop a system, including database and radiation dosimetry badges, for monitoring and registering radiation exposure (dose) of health care providers during interventional radiologic procedures (e.g., angioplasty, percutaneous renal stone removal).

D. Develop a context-sensitive audio and video user assistance or training system that can be temporarily attached or permanently integrated with a moderately complex medical device such as an IV pump, defibrillator, or ventilator. Its ability to address the use of these devices in the home environment is advantageous.

CENTER FOR VETERINARY MEDICINE (CVM)

CVM is a public health organization that enables the marketing of effective drugs, food additives, feed ingredients, and animal devices that are safe to animals, humans, and the environment. The Center, in partnership with Federal and state agencies and other customers, ensures animal health and the safety of food derived from animals. The Center makes timely, quality decisions and takes regulatory actions to ensure that these products provide for quality health care of animals, minimize the transmission of zoonotic diseases, and increase the efficiency of production of animal-derived food and fiber. Regulatory decisions are supported by research, the monitoring of product safety, and efficacy, and the continual improvement of processes.

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

The Office of Orphan Products Development was established to identify and facilitate the development of orphan products. Orphan products are drugs, biologics, medical devices and foods for medical purposes, which are indicated for a rare disease or condition (i.e., one affecting fewer than 200,000 people in the United States). These products may be useful in a rare disease/disorder but lack commercial sponsorship because they are not considered commercially attractive for marketing. A subcategory of orphan products are those marketed products in which there is evidence suggesting usefulness in a rare disease/disorder but which are not labeled for that disease/disorder because substantial evidence of safety and effectiveness for that use is lacking.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Development of pediatric formulations for already approved products for the specific purpose of submitting data to the FDA to include pediatric labeling to the current label of the approved product.

B. Development of products for the treatment of rare diseases or disorders including but not limited to neurological, metabolic, genetic, ophthalmologic, hematologic, and dermatological diseases or disorders for the specific purpose of obtaining marketing licensure.

C. Development of products for use in diagnosis of rare diseases for which the diagnostic tool would be used in fewer than 200,000 persons annually in the United States.

D. Development of vaccines for the prevention of rare diseases to be used in fewer than 200,000 persons annually in the United States.

Other Research Topic(s) Within the Mission of FDA

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