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

SMALL BUSINESS INNOVATION RESEARCH (SBIR)

AND

SMALL BUSINESS TECHNOLOGY TRANSFER (STTR)

GRANT APPLICATIONS

NIH, CDC, FDA, and ACF Program Descriptions and Research Topics

SUBMISSION DATES

APRIL 5, AUGUST 5, AND DECEMBER 5, 2014

(MAY 7, SEPTEMBER 7, 2014 AND JANUARY 7, 2015 FOR AIDS/AIDS-RELATED RESEARCH)

National Institutes of Health (SBIR and STTR)

Centers for Disease Control and Prevention (SBIR)

Food and Drug Administration (SBIR)

Administration for Children and Families (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

REMINDER: ALL APPLICATIONS MUST BE SUBMITTED IN RESPONSE TO A FUNDING OPPORTUNITY ANNOUNCEMENT THROUGH GRANTS.GOV

SMALL BUSINESS INNOVATION RESEARCH PROGRAM PARENT ANNOUNCEMENT (SBIR [R43/R44]) HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-14-071.HTML

SMALL BUSINESS TECHNOLOGY TRANSFER PROGRAM PARENT ANNOUNCEMENT (STTR [R41/R42]) HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-14-072.HTML

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

APPLICATION INSTRUCTIONS

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

APPENDICES

STTR MODEL AGREEMENT (MS WORD)

EXTRAMURAL INVENTION REPORTING COMPLIANCE RESPONSIBILTIES (HTTPS://S-EDISON.INFO.NIH.GOV/IEDISON/TIMELINE.JSP)

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 (i.e., Institutes and Centers (ICs)) identified in this solicitation.

Applicants are strongly encouraged to subscribe to the NIH Guide for Grants and Contracts LISTSERV (http://grants.nih.gov/grants/guide/listserv.htm) or query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, FDA, and ACF awarding components.

You may also subscribe to the SBIR-STTR LISTSERV list to get timely information about the NIH SBIR/STTR Programs (http://grants.nih.gov/grants/funding/listserv.htm).

Additional information on each of the awarding components (ICs) 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)

NIH is the steward of medical and behavioral research for the Nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.

The goals of the agency are as follows:

1. to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health;
2. to develop, maintain, and renew scientific human and physical resources that will assure the Nation's capability to prevent disease;
3. to expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and
4. to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

In realizing these goals, the NIH provides leadership and direction to programs designed to improve the health of the Nation by conducting and supporting research:

- in the causes, diagnosis, prevention, and cure of human diseases;
- in the processes of human growth and development;
- in the biological effects of environmental contaminants;
- in the understanding of mental, addictive and physical disorders; and
- in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists.

In addition, the NIH sponsors training of research personnel; career development of new and established scientists; construction and renovation of research facilities and provision of other research resources.

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 applications, including the co-funding of such applications by one or more awarding components having relevance in the projects.

Funding levels for projects are determined through the combined interaction among peer review, grants management, program, budget, and other Institute and/or Centers (IC) staff. These levels are based on allowable costs that are consistent with the principles of sound cost management and in consideration of IC priorities, constraints on the growth of average grant costs, and the availability of funds.

Before considering and/or preparing an application to the SBIR & STTR programs, all applicants are **strongly encouraged** to review the agencies' and NIH Institutes' and Centers' websites and to contact the SBIR-STTR program coordinators listed in the Omnibus Solicitation.

TRANS-NIH RESEARCH PROGRAMS

Phase IIB Competing Renewal Awards

Some NIH Institutes/Centers (ICs) offer Phase II SBIR/STTR awardees the opportunity to apply for Phase IIB Competing Renewal awards. These are available for those projects that require extraordinary time and effort in the R&D phase and may or may not require FDA approval for the development of such projects, including drugs, devices, vaccines, therapeutics, and medical implants related to the mission of the IC. Some ICs have announced this opportunity through the NIH Guide for Grants and Contracts (see link 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 IIB Competing Renewal award. Prospective applicants are strongly encouraged to contact NIH staff prior to submission. 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 Funding Opportunity Announcements (http://grants.nih.gov/grants/funding/sbir_announcements.htm). The following NIH ICs will accept applications for Phase IIB Competing Renewal awards: **NIA, NIAAA, NIAID** (SBIR only)**, NICHD** (SBIR only and only Competing Renewals of NICHD-supported Phase II awards)**, NIDA, NIDCD, NIDDK** (only Competing Renewals of NIDDK-supported Phase II awards**), NEI, NIGMS** (SBIR only), **NIMH** (SBIR only), **NCATS** (SBIR only), and **ORIP** (SBIR only). **NCI** offers Phase IIB opportunities that focus on the commercialization of SBIR-developed technologies. Contact the NCI SBIR Development Center at 301-594-7709, NCISBIR@mail.nih.gov for additional information. NHLBI offers Phase IIB Competing Renewals that focus on the commercialization of technologies requiring regulatory approval through the **NHLBI** Bridge Award (RFA-HL-13-016). Contact Kurt Marek, Ph.D., at 301-443-8778 or kurt.marek@nih.gov for additional information. **NINDS** accepts Phase IIB SBIR/STTR Competing Renewal applications through specific opportunities that focus on the commercialization of SBIR and STTR developed technologies. These opportunities can be found on the NINDS SBIR webpage: http://www.ninds.nih.gov/funding/small-business/small_business_funding_opportunities.htm. Contact Stephanie Fertig, M.B.A., at 301-496-1779 or fertigs@ninds.nih.gov for additional information.

Research Supplements to Promote Diversity in Health-Related Research

(See Funding Opportunity Announcement at http://grants.nih.gov/grants/guide/pa-files/PA-12-149.html.)

The NIH recognizes a unique and compelling need to promote diversity in the biomedical, behavioral, clinical and social sciences research workforce. The NIH expects efforts to diversify the workforce to lead

to the recruitment of the most talented researchers from all groups; to improve the quality of the educational and training environment; to balance and broaden the perspective in setting research priorities; to improve the ability to recruit subjects from diverse backgrounds into clinical research protocols; and to improve the Nation's capacity to address and eliminate health disparities.

The NIH notifies Principal Investigators holding specific types of NIH research grants (including SBIR and STTR awards) that funds are available for administrative supplements to improve diversity by supporting and recruiting students, postdoctorates, and eligible investigators from groups that have been shown to be underrepresented in the biomedical, behavioral, clinical, and social sciences research workforce. Although the administrative supplements supported under this program provide funding for less than one percent of all individuals involved in NIH supported research, the NIH has found these awards to be an effective means of encouraging institutions to recruit from currently underrepresented groups. Further information on the NIH diversity policy and the groups that have been identified as underrepresented in biomedical research can be found at http://grants.nih.gov/training/faq_diversity.htm. Administrative supplements must support work within the scope of the original project.

All NIH awarding components and the National Institute for Occupational Safety and Health at the CDC participate in this program. Candidates eligible for support under this supplement program include individuals at various career levels who come from groups that have been shown to be underrepresented in science. Such candidates include individuals from underrepresented racial and ethnic groups, individuals with disabilities, and individuals from disadvantaged backgrounds. Detailed eligibility criteria are described in the full announcement.

An application for a supplement may be submitted at any time. Administrative supplements normally end with the competitive cycle of the parent grant.

TECHNICAL ASSISTANCE PROGRAMS (SUBJECT TO CHANGE)

Available to NIH SBIR/STTR Awardees

One of the goals of the SBIR and STTR programs is to “increase private sector commercialization of innovations developed through Federal Research and Development.” To help NIH SBIR/STTR awardees move their products into the marketplace, NIH has developed assistance programs that provide technical and/or commercialization assistance specific to the individual needs of NIH SBIR/STTR awardees. In accordance with the SBIR/STTR Reauthorization Act of 2011, applicants can also identify and utilize their own technical assistance vendor, however they are required to include this as a consultant in the budget section with a detailed budget justification. See SF424 (R&R) SBIR/STTR Application Guide for instructions. Please note, if funds are requested to utilize your own technical assistance vendor and an award is made, the awardee cannot apply for the NIH-provided technical assistance program for the phase of their award.

Additional information about these programs is available at http://grants.nih.gov/grants/funding/tap.htm. Questions may be addressed to the NIH SBIR/STTR Office at sbir@od.nih.gov.

Niche Assessment Program

(FOR NIH SBIR/STTR PHASE I AWARDEES)

The Niche Assessment Program focuses on providing strategic information about the technology’s market and customer opportunities. Often, a research scientist does not have the entrepreneurial skills to assess whether there are other applications or market niches for their SBIR/STTR-developed technology. As a result, they may underestimate its true market value. This program assesses the market opportunities, needs and concerns of end-users and helps to discover new markets for possible entry for the SBIR/STTR-developed technology. With the assistance of the participant, a contractor helps identify

niches and potential partners. The contractor performs the due diligence and provides an in-depth report that assesses such items as the potential end-users needs, the competing technologies and products, the competitive advantage, the market size and share that the participant might expect, etc. Targets (end users) are contacted to ensure they are viable leads and their contact information is included in the report for possible follow-up. Participants may find this report helpful in preparing the requisite Commercialization Plan required for a Phase II application. For detailed information about the Niche Assessment Program, see http://grants.nih.gov/grants/funding/nap.htm.

Participation in this program is open to active NIH SBIR and STTR Phase I awardees (grants, cooperative agreements, and contracts) and participants need only commit a few hours to inform and make the contractor fully conversant on their technology and the niche they would like to have investigated. There is no cost to the NIH awardee to participate in this program.

Commercialization Assistance Program (CAP)

(FOR NIH SBIR/STTR PHASE II AWARDEES)

The Commercialization Assistance Program (CAP) assists small companies with getting their SBIR/STTR-developed technologies more rapidly into the marketplace. It provides assistance with developing and implementing an appropriate business strategy aimed at commercializing the products or services that have resulted from NIH-supported SBIR/STTR awards.

CAP can include distinctive tracks that offer customized assistance to meet the specific needs of both early stage and seasoned companies: 1) Emerging company track, 2) Advanced company track, and 3) Regulatory assistance track. The emerging track is aimed at assisting participants with evaluating their commercialization options based on their specific technologies and to develop a solid market-entry plan covering an 18-month period. It also assists in the development of market-appropriate tools to accomplish these objectives.

The advanced track assists those companies that may have successfully commercialized products and/or services, generated revenue, established partnerships and/or otherwise achieved a level of market development that is sustainable over a definitive period. However, they may be lacking in a specific, applicable issue (such as a license-focused IP strategy or a term sheet for investors), whose resolution is key to their continued growth.

The regulatory track is focused on providing individualized assistance to those companies whose technologies must go through the Food and Drug Administration (FDA) approval process and, therefore, seek help in developing a sound regulatory plan and strategy to navigating the regulatory landscape.

Participation in CAP is open to NIH SBIR and STTR Phase II awardees (grants, cooperative agreements, and contracts) from the previous five years. Participation is free to the NIH SBIR/STTR awardee; however, participants are responsible for travel and lodging expenses associated with attending workshops and partnering events. Detailed information about the CAP is available at http://grants.nih.gov/grants/funding/cap/index.htm.

NIH, CDC, FDA, AND ACF AWARDING COMPONENT CONTACT INFORMATION

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute on Aging http://www.nia.nih.gov	Dr. Michael-David A.R.R. Kerns Phone: 301-402-7713 Fax: 301-402-2945 Email: Michael-David.Kerns@nih.gov	Ms. Linda Whipp Phone: 301-496-1472 Fax: 301-402-3672 Email: Linda.Whipp@nih.gov
National Institute on Alcohol Abuse and Alcoholism http://www.niaaa.nih.gov	Dr. Kathy Jung Phone: 301-443-8744 Fax: 301-594-0673 Email: Kathy.jung@nih.gov	Ms. Judy Fox Phone: 301-443-4704 Fax: 301-443-3891 Email: Judy.Fox@nih.gov
National Institute of Allergy and Infectious Diseases http://www.niaid.nih.gov	Dr. Natalia Kruchinin Phone: 301-496-8666 Fax: 301-496-8729 Email: kruchininn@niaid.nih.gov	Ms. Deanna L. Ingersoll Phone: 301-451-2686 Fax: 301-493-0597 Email: ingersolld@niaid.nih.gov Ms. Artisha Wright Phone: 301-496-7065 Fax: 493-0597 Email: Artisha.Wright@nih.gov
National Institute of Arthritis and Musculoskeletal and Skin Diseases http://www.niams.nih.gov/	Dr. Xibin Wang Phone: 301-451-3884 Fax: 301-480-1284 Email: wangx1@mail.nih.gov	Mr. Erik (Timothy) Edgerton Phone: 301-594-3968 Fax: 301-480-5450 Email: edgertont@mail.nih.gov
National Institute of Biomedical Imaging and Bioengineering http://www.nibib.nih.gov/	Mr. Todd Merchak Phone: 301-496-8592 Fax: 301-480-1614 Email: merchakt@mail.nih.gov	Mr. James Huff Phone: 301-451-4786 Fax: 301-451-5735 Email: huffj@mail.nih.gov
National Cancer Institute http://sbir.cancer.gov	Mr. Michael Weingarten Dr. Greg Evans Dr. Andrew Kurtz Phone: 240-276-5300 Fax: 240-276-5236 Email: ncisbir@mail.nih.gov	Ms. Jacquelyn Boudjeda Phone: 240-276-6312 Fax: 240-276-7913 Email: boudjedaj@mail.nih.gov
Eunice Kennedy Shriver National Institute of Child Health and Human Development http://www.nichd.nih.gov	Louis A. Quatrano, Ph.D. Phone: 301-402-4221 Fax: 301-402-0832 Email: Quatranol@mail.nih.gov	Mr. Ted Williams Phone: 301- 435-6996 Fax: 301- 451-5510 Email: williate@mail.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute on Drug Abuse http://www.nida.nih.gov	Elena Koustova, Ph.D., MBA Phone: 301-496-8768 Email: koustovae@nida.nih.gov	Ms. Diana Haikalis, M.B.A. Phone: 301-443-6710 Fax: 301-594-6849 Email: dhaikali@nida.nih.gov
National Institute on Deafness and Other Communication Disorders http://www.nidcd.nih.gov	Dr. Roger L. Miller Phone: 301-402-3458 Fax: 301-402-6251 Email: Roger.Miller@nih.gov	Mr. Christopher P. Myers Phone: 301-435-0713 Fax: 301-402-1758 Email: Christopher.Myers@nih.gov
National Institute of Dental and Craniofacial Research http://www.nidcr.nih.gov	Dr. R. Dwayne Lunsford Phone: 301-594-2421 Fax: 301-480-8319 Email: lunsfordr@mail.nih.gov	Ms. Diana Rutberg Phone: 301-594-4798 Fax: 301-480-3562 Email: rutbergd@mail.nih.gov
National Institute of Diabetes and Digestive and Kidney Diseases http://www.niddk.nih.gov	Ms. Christine Densmore Phone: 301-402-8714 Fax: 301-480-8300 Email: densmorec@niddk.nih.gov	Mr. Gene McGeehan Phone: 301-594-0417 Fax: 301-594-9523 Email: mcgeehane@niddk.nih.gov
National Institute of Environmental Health Sciences http://www.niehs.nih.gov	Dr. Daniel T. Shaughnessy Phone: 919-541-2506 Fax: 919-541-4606 Email: shaughn1@niehs.nih.gov	Ms. Pam Clark Phone: 919-541-7629 Fax: 919-541-2860 Email: evans3@niehs.nih.gov
National Eye Institute http://www.nei.nih.gov	Dr. Jerome Wujek Phone: 301-451-2020 Fax: 301-496-2297 Email: wujekjer@nei.nih.gov	Mr. William Darby Phone: 301-451-2020 Fax: 301-496-9997 Email: darbyw@nei.nih.gov
National Institute of General Medical Sciences http://www.nigms.nih.gov/	Dr. Scott Somers Phone: 301-594-3827 Fax: 301-480-2802 Email: somerss@nigms.nih.gov	Ms. Patrice Molnar Phone: 301-594-5136 Fax: 301-480-2554 Email: molnarp@nigms.nih.gov
National Heart, Lung, and Blood Institute http://www.nhlbi.nih.gov	Kurt Marek, Ph.D. Phone: 301-443-8778 Fax: 301-480-0422 Email: Kurt.Marek@nih.gov	Andre Walker Phone: 301-435-0166 Fax: 301-451-5462 Email: Andre.Walker@nih.gov Hubert Walters Phone: 301-435-0166 Fax: 301-451-5462 Email: waltersh@nhlbi.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Human Genome Research Institute http://www.genome.gov	Dr. Michael W. Smith Phone: 301-496-7531 Fax: 301-480-2770 Email: smithmw@mail.nih.gov	Ms. Cheryl Chick Phone: 301-435-7858 Fax: 301-402-1951 Email: ChickC@mail.nih.gov
National Institute of Mental Health http://www.nimh.nih.gov	Dr. Margaret C. Grabb Phone: 301-443-3563 Fax: 301-443-1731 Email: mgrabb@mail.nih.gov	Ms. Rebecca Claycamp Phone: 301-443-2811 Fax: 301-443-6885 Email: rclaycam@mail.nih.gov
National Institute on Minority Health and Health Disparities http://www.nimhd.nih.gov/	Mr. Vincent A. Thomas, Jr. MSW, MPA Phone: 301-402-2516 Fax: 301-480-4049 Email: thomasvi@mail.nih.gov	Ms. Priscilla Grant, J.D., C.R.A. Phone: 301-594-8412 Fax: 301-480-4049 Email: Priscilla.Grant@nih.gov
National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov	Ms. Stephanie Fertig Phone: 301-496-1779 Fax: 301-402-1501 Email: fertigs@ninds.nih.gov	Ms. Tijuanna Decoster Phone: 301-496-9231 Fax: 301-402-4370 Email: decostert@mail.nih.gov
National Institute of Nursing Research http://www.nih.gov/ninr	Dr. Paul A. Cotton Phone: 301-402-6423 Fax: 301-480-8260 Email: Paul.Cotton@nih.gov	Mr. Brian Albertini Phone: 301-594-6869 Fax: 301-402-4502 Email: albertib2@mail.nih.gov
National Center for Advancing Translational Sciences http://www.ncats.nih.gov	Lili M. Portilla, MPA Phone: 301-402-0304 Fax: 301-480-3661 Email: Portilll@mail.nih.gov	Mrs. Tiffany Walker Phone: 301-402-0839 Fax: 301-480-3777 Email: walkerti@mail.nih.gov
National Center for Complementary and Alternative Medicine http://www.nccam.nih.gov/	Dr. Craig Hopp Phone: 301-496-5825 Fax: 301-480-1587 Email: hoppdc@mail.nih.gov	Mr. George Tucker, MBA Phone: 301-594-8853 Fax: 301-480-1552 Email: George.Tucker@nih.gov
National Library of Medicine http://www.nlm.nih.gov	Dr. Jane Ye Phone: 301-594-4882 Fax: 301-402-2952 Email: yej@mail.nih.gov	Mr. Dwight Mowery Phone: 301-496-4221 Fax: 301-402-0421 Email: moweryd@mail.nih.gov
Division of Program Coordination, Planning, and Strategic Initiatives, Office of Research Infrastructure Programs http://dpcpsi.nih.gov/ORIP/index.aspx	Dr. Miguel Contreras Phone: 301-594-9410 Fax: 301-480-3819 Email: contre1@mail.nih.gov	Mr. Long Nguyen Phone: 301-402-6737 Fax: 301-480-3777 Email: nguyen1@mail.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
Centers for Disease Control and Prevention (CDC) http://www.cdc.gov	Dr. Ron Ballard (CGH) Phone: 404-639-2143 Fax: 404-639-7490 Email: RBallard@cdc.gov Mr. Sean Griffiths (CSELS) Phone: 404-639-4641 Fax: 404-639-4903 Email: SGriffiths@cdc.gov Dr. Brenda Colley Gilbert (NCBDDD) Phone: 770-488-8390 Fax: 770-488-7863 Email: BColleyGilbert@cdc.gov Ms. Barbara Stewart (NCEZID, NCHHSTP) Phone: 404-718-8832 Fax: 404-498-2626 Email: BStewart@cdc.gov Dr. Paul Smutz (NCIPC) Phone: 770-488-4850 Fax: 770-488-1665 Email: WSmutz@cdc.gov Dr. Steve Dearwent (NIOSH) Phone: 404-498-6382 Fax: 404-498-0751 Email: SDearwent@cdc.gov	Angie Tuttle (CGH) Phone: 770-488-2863 Fax: 770-488-2777 Email: ATuttle@cdc.gov Mr. Hector Buitrago (CGH) Phone: 770-488-2921 Fax: 770-488-2777 Email: HBuitrago@cdc.gov Ms. Devi Hawkins (CSELS) Phone: 770-488-2543 Fax: 770-488-2670 Email: DHawkins@cdc.gov Roslyn Curington (NCBDDD) Phone: 770-488-2745 Fax: 770-488-2777 Email: RCurington@cdc.gov Tracey Sims (NCBDDD) Phone: 770-488-2739 Fax: 770-488-2777 Email: TraceySims@cdc.gov Anella Higgins(NCEZID) Phone: 770-488-2710 Fax: 770-488-8350 Email: AHiggins@cdc.gov Edna Green (NCHHSTP) Phone: 770-488-2858 Fax: 770-488-2828 Email: EGreen@cdc.gov Mr. Ralph Robinson (NCIPC) Phone: 770-488-2441 Fax: 770-488-2847 Email: RRobinson6@cdc.gov Ms. Mary Pat Shanahan (NIOSH) Phone: 412-386-4453 Fax: 412-386-6429 Email: MShanahan@cdc.gov
Food and Drug Administration (FDA) http://www.fda.gov	Ms. Kimberly Pendleton Chew Phone: 301-827-9363 Fax: 301-827-0505 Email: kimberly.pendleton@fda.hhs.gov	Mr. Martin Bernard Phone: 301-443-5869 Fax: 301-827-0505 Email: Martin.Bernard@fda.hhs.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
Administration for Children and Families http://www.acf.hhs.gov	Anne F. Bergan Phone: 202-260-8515 Fax: 202-205-3598 Email: abergan@acf.hhs.gov	Edeltraud Fernandez Phone: 202-401-2346 Fax: 202-205-3598 Email: efernandez@acf.hhs.gov

NATIONAL INSTITUTE ON AGING (NIA)

The NIA SBIR-STTR Programs support 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 SBIR and STTR grant research under four established divisions: Behavioral and Social Research, Aging Biology, Geriatrics and Clinical Gerontology, and Neuroscience.

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.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, the NIA may not fund an application or may decrease the length of an award and/or the budget recommended by a review committee. For topics listed in APPENDIX A: National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations, the NIA does not generally fund Phase I applications greater than $300,000 total costs or project periods greater than 2 years; or Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years. For all other topics, the NIA does not generally fund Phase I applications greater than $225,000 total costs or project periods greater than 2 years; or Phase II applications greater than $1,500,000 total costs or project periods greater than 3 years. Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB Competing Renewal Awards

NIA accepts Phase IIB Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing aging- and health-focused products, including pharmaceutical compounds and medical devices. NIA accepts applications for up to two (2) years and up to $750,000 per year in total costs. The Phase IIB Competing Renewal award is intended to allow small businesses the opportunity to advance research to a stage where interest in and investment by third parties would be more likely.

Prospective Phase IIB Competing Renewal applicants are strongly encouraged to submit via email a letter of intent to Dr. Kerns 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
- Anticipated Budget
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-12-XXX, if relevant)

Although a letter of intent is not binding and does not enter into the review of a subsequent application, it allows NIA staff to estimate the potential review workload, plan the review, and consider budget implications. It is anticipated that only a small number of NIA SBIR/STTR Phase II awards would be eligible for a Phase IIB Competing Renewal award.

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

Dr. Michael-David ("M-D") A.R.R. Kerns
301-402-7713, Fax: 301-402-2945

Email: kernsmd@mail.nih.gov

Division of Behavioral and Social Research (DBSR)

Basic and translational social and behavioral research on aging processes and the place of older people in society. The division focuses on how people change with age, on the interrelations 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. Special emphasis areas are (1) Health Disparities; (2) Aging Minds; (3) Increasing Health Expectancy; (4) Health, Work, and Retirement; (5) Interventions and Behavior Change; (6) Genetics, Behavior, and the Social Environment; and (7) the Burden of Illness and the Efficiency of Health Systems.

LIMITED AMOUNT OF AWARD

For budgetary, administrative, or programmatic reasons, NIA 's Division of Behavioral and Social Research (DBSR) may not fund an SBIR or STTR application or may decrease the budget and duration of an award recommended by a peer-review committee. Generally, NIA DBSR does not fund Phase I applications with budgets greater than $150,000 or Phase II applications with budgets greater than $1,000,000.

In making funding decisions about SBIR and STTR applications recommended by a peer-review committee, NIA DBSR emphasizes proposals that feature new and innovative research and development. Furthermore, NIA DBSR places a premium on innovative SBIR-STTR research and development that address new and different product categories, product categories that transcend traditional categories of focus, such as training videos and medication reminders.

Applicants considering requested budgets greater than these limits or for research and development of training videos or medication reminders are strongly encouraged to contact NIA DBSR program staff prior to developing and submitting SBIR-STTR applications.

A. Development and translation of behavioral economics approaches (incentives or disincentives) to motivate sustainable behavior change to improve health and well-being.
    1. Increasing levels of physical activity or promoting treatment adherence
    2. Addressing biases such as loss aversion, errors in affective forecasting, present bias, ambiguity effect, base-rate neglect, and susceptibility to framing effects in health and financial decision making
    3. Using information, or the mode of data presentation to systematically improve decision making (e.g., through "nudges," policies, or practices that constrain choices)

B. Development of robotics applications to aid elderly
    1. Socially assistive robots allowing elderly to remain independent in their homes. Technology could support machine cognition, language understanding and production, human-robot interaction (cognition, perception, action control, linguistics, and developmental science), perception, and systems.
    2. Use of robots to motivate elderly to exercise and improve social interaction

C. Development of cognitive training applications/intervention to improve cognitive function in elderly
    1. Rapidly develop novel, engaging computer-based cognitive training programs that are based on efficacious approaches and which use cognitive training to target a specific neural system/functional domain.
    2. Augment existing computerized cognitive interventions to be personalized, engaging, adaptive, sufficiently challenging, and optimal for maximizing real world functional improvements.

D. Social, behavioral, environmental and or/technical interventions on the individual, institutional, family, community or national level intended to maintain older adult independence or functioning, increase well-being and prevent disease and/or disability.

   1. Interventions to remediate age-related cognitive decline, especially using technology platforms with wide acceptance among older adults;
   2. Interventions directed at self-management of chronic diseases among the elderly, including behavioral change and applications to enhance compliance;
   3. Interventions to enhance social function or to improve physical and psychological well-being in midlife and older age;
   4. The development of evidence-based, risk-reduction programs (also referred to as health promotion, health management, demand management, and disease-prevention programs) that are applicable to older U.S. workers.

E. Genetics and Genome Wide Association

   1. Development of innovative methods and software to facilitate analysis of personal data linked to geocoded data, biological, cognitive or genetic measures, with improved protection for confidentiality.
   2. Develop online genetic counseling so that users have a way to interface with professionals regarding issues that may have arisen after learning about genetic risk for disease, or about any new ancestry information that might be at odds with their self-identified race.
   3. Develop a more targeted understanding of who will engage in DTC genetic testing and who will not, based on personality and other characteristics. This could be accomplished through comparisons with other large-scale surveys.

Contact Person: Partha Bhattacharyya
301-496-3138, Fax: 301-402-0051
Email: bhattacharyyap@nia.nih.gov

F. Devices, products, services or technology that would assist the elderly and their families or caregivers during disasters and recovery from disasters.

G. The development of software to improve financial decision making among older people. The software should include projected retirement earnings and expenditures on long term care and out of pocket medical expenditures.

H. The development of practical applications using innovative technologies (hand-held, internet, telemedicine GPS, social networking and communications technologies) to support and improve quality of life, well-being, and the ability of older adults to live independently and safely at home).

I. New sampling and data collection methodologies for use in large population-based household surveys and behavioral interventions of relevance to aging. These include:

   1. Experience sampling and new devices for real-time collection of data;
   2. Performance based measures for cognitive or physical functioning as well as new instruments for cognitive testing, sleep quality, assessment of basic decision-making domains, or assessments of social behaviors;
   3. Improvements to blood spot technology for biological data collection (this includes the development of multiple and reliable assays for limited blood spot specimens).

J. Survey Development/Archiving/Database support

1. Development of new databases and database support infrastructure to satisfy data and research needs in aging as well as the development of innovative data archives to make current statistical and epidemiological data more accessible and policy relevant;
2. Development of data extraction web tools for public use databases;
3. Development of innovative methods and software to provide improved access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality;
4. Development of innovative methods and software to facilitate analysis of personal data linked to geocoded data, biological, cognitive or genetic measures, with improved protection for confidentiality of respondents;
5. Development of data infrastructure and tools for assessing the economic impact of federally-funded research.

K. Forecasting and Software for analyzing of healthcare claims

1. Development of 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 costs and effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. Both domestic and international projections are of interest;
2. Development of software which will provide insight on key factors that contributes to growth of medical expenditures through analysis of claims data.

L. Develop risk reduction programs (also referred to as health promotion, health management, demand management, and disease prevention programs) among those aged 45-64 within the private sector or health. The goal of these interventions is to improve the health of older workers, reduce avoidable health care utilization, and be cost-effective for employee insurance plans.

Contact Person: Ms. Farheen Akbar
301-402-4156, Fax: 301-402-0051
Email: farheen.akbar@nih.gov

Division of Aging Biology (DAB)

DAB sponsors research on the molecular, cellular, genetic, and physiological causes and consequences of aging processes. The ultimate goal is to develop interventions to reduce and/or delay age-related degenerative processes in humans. DAB 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 including, for example, human fetal lung fibroblasts.

DAB areas of research 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-oxidants or other interventions to reduce oxidative or other stresses and aging-related diseases.

Dr. David Finkelstein
Phone: 301-496-6402
Email: df18s@nih.gov

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
Phone: 301-496-6402
Email: nadonn@nia.nih.gov

C. 1. 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*.

2. Validation and further development of candidate interventions which have been found to enhance longevity or slow aging, either in cultured cells, animal models, and humans, and which may affect other age-related conditions or diseases such as cancer and cardiovascular diseases.

3. Development of interventions that improve the immune response to foreign molecules or reduce the response to self or suppress age-induced inflammation.

Dr. Rebecca Fuldner
Phone: 301-496-6402
Email: Fuldnerr@mail.nih.gov

D. Development of novel strategies for treating age-related renal, pulmonary, urology, reproductive disorders, and age-related changes in hormone production and function. The topics could include devices, pharmacological targets and their validation, small molecules and other approaches to treat these disorders in the elderly. Early-stage pharmacological validation of novel targets and accompanying pre-therapeutic leads for these age-related diseases are encouraged.

Dr. Mahadev Murthy
Phone: 301-496-6402
Email: murthy@mail.nih.gov

E. 1. Development of treatments for wound healing in the aged. These would include devices, processes, and pharmacological agents with the potential to (1) promote would healing in aged tissues, or (2) reduce scar formation without compromising effective healing. Wounds produced by accidental damage or resulting from surgery would be appropriate for consideration.

2. Development of novel methodology for treating osteoarthritis. These could include devices, processes and pharmacological agents with the potential to (1) Slow the rate of joint deterioration, (2) promote the remodeling of damaged joints, (3) reduce the likelihood of progression to osteoarthritis, and/or (4) improve outcomes for patients with active osteoarthritis.

3. Development of anabolic treatments to delay bone loss and or promote new bone deposition for the treatment of metabolic bone disorders.

Dr. John Williams
Phone: 301-496-6402
Email: williamsj6@mail.nih.gov

F. 1. Development of cell-based therapies or other treatments to repair myocardial or vascular tissues after ischemia. The work should include consideration of age-related effects on the therapy or treatment.

2. Early development to re-purpose FDA-approved drugs or interventions for common diseases (cancer, cardiovascular, etc.) on aging-related diseases or conditions using senescence cell culture or animal models.

Dr. Ronald Kohanski
Phone: 301-496-6402
Email: kohanskir@mail.nih.gov

G. 1. Development of tools and technologies to characterize cellular heterogeneity in aging tissues at the single cell level.

2. Development of interventional strategies to alter the senescence status of cells in tissues and organs of old animals.
3. Development of computational and bio statistical methods for systems biology approaches.
4. Development of new interventions using screens for senescence in cell culture or animal models.
5. Development of interventions that reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, and improve the damage surveillance and repair potential of cells.

Dr. Jose Velazquez
Phone: 301-496-6402
Email: Jose.Velazquez@nih.gov

H. 1. Development of tools and resources in genetics and genomics to study molecular mechanisms of normal aging or aging-related diseases.

2. Development of biomarkers for prognosis, diagnosis, or treatment monitoring of aging or aging-related diseases. Analysis and integration of large data sets are encouraged for developing such biomarkers or biomarker signatures.
3. Development of computational, statistical, or bioinformatics tools and resources to manage, integrate, and mine large aging-related data sets; Development of databases, methods, or data analysis systems for aging research; Development of technologies, tools, methods, and resources useful for the study of aging and aging-related diseases at the systems biology level.
4. Development of probiotics or prebiotics which are beneficial for age-related diseases or conditions.

Dr. Max Guo
Phone: 301-402-7747
Email: Max.Guo@nih.gov

Division of Neuroscience (DN)

DN supports 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, sleep and circadian rhythms, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, motor, perceptual, cognitive and affective processes and changes that occur with aging as related to their underlying biological mechanisms.

An important component of DN is the support of studies on Mild Cognitive Impairment (MCI), Alzheimer's disease (AD), and other dementias of aging such as Frontotemporal Dementia, Lewy Body Dementia, and Vascular Dementia.

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

A. Development of sensitive, specific and standardized tests for diagnostic screening of MCI and dementia; for example, the development of novel neuropsychological, biochemical and neuroimaging methods for the early detection of cognitive impairment and MCI and the early diagnosis of AD, and development of new tests for detection of pre-clinical AD.

Dr. John Hsiao (neuroimaging, biomarkers of MCI, AD)
301-496-9350; Fax: 301-496-1494
Email: jhsiao@mail.nih.gov

or

Dr. Nina Silverberg (neuropsychological detection methods in MCI, AD)
301-496-9350; Fax: 301-496-1494
Email: silverbergn@mail.nih.gov

or

Dr. Molly Wagster (neuroimaging or neuropsychological detection methods in pre-clinical AD)
301-496-9350; Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

B. Discovery, development, and/or evaluation of drugs, biological or natural products, including central-nervous-system delivery systems to remediate age-related cognitive decline, and to treat the cognitive impairment and/or behavioral symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of the disease or to prevent it entirely.

Dr. Larry Refolo (Alzheimer's disease & other dementias of aging)
301-496-9350, Fax: 301-496-1494
Email: refolol@mail.nih.gov

or

Dr. Molly Wagster (age-related cognitive decline)
301-496-9350; Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

C. The development of practical applications using innovative technologies (e.g. hand-held, internet, telemedicine GPS, robotics, social networking and communications technologies) to support and improve quality of life, well-being, and the ability of people with MCI, AD or other dementias of aging to live independently and safely at home for an extended period of time. Examples include systems and devices to: evaluate, monitor and improve or adapt to changes in cognition; improve health service delivery; support independent living and the conduct of everyday tasks at home; provide information to health care providers and family members with which to evaluate the need for intervention; and promote communication and interaction between individuals living in the community or in institutional settings and their health care providers, friends and family members.

Dr. Nina Silverberg
301-496-9350; Fax: 301-496-1494
Email: silverbergn@mail.nih.gov

D. Testing in clinical trials of drug, nutritional, behavioral, cognitive or other types of interventions to remediate age-related cognitive decline, and to treat cognitive impairment and/or behavioral symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of disease or to prevent the onset of disease.

Dr. Laurie Ryan (MCI, AD, & other dementias of aging)
301-496-9350; Fax: 301-496-1494
Email: ryanl@mail.nih.gov

or

Dr. Molly Wagster (age-related cognitive decline prevention)
301-496-9350; Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

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

F. Behavioral, environmental, pharmacological, & nutritional interventions to prevent and/or remediate brain biochemical and/or neurophysiological changes caused by normal aging and neurodegenerative diseases, including age-related sensory dysfunction (e.g., pain, hearing loss, speech communication disorders, olfaction loss, & vision loss), motor dysfunctions (including Parkinson's disease & other age-related psychomotor disorders) or age-related decrements in balance & postural control, gait performance, and mobility.

G. Biosensors and prosthetic devices, technologies, and related software development to aid in the assessment, diagnosis, and remediation of age-related cognitive decline or sensory dysfunction (including pain, age-related vision loss, and age-related hearing loss), motor dysfunction (including Parkinson's disease and other motor disorders of aging), or age-related changes in balance, postural control, and gait. Novel markers of normal age-dependent cognitive decline or sensory and/or motor system changes at the molecular cellular, circuitry, physiological or behavioral level in humans or relevant animal models.

Dr. Wen G. Chen (motor, sensory)
301-496-9350, Fax: 301-496-1494
Email: chenw@mail.nih.gov

or

Dr. Molly Wagster (cognition)
301-496-9350, Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

H. 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.

I. Minimally invasive technologies to detect prion diseases early in the course of the disease process in older adults, as well as effective treatment strategies to slow, halt or prevent these diseases.

Dr. Miroslaw Mackiewicz
301-496-9350, Fax: 301-496-1494
Email: mackiewiczm2@mail.nih.gov

J. 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 animals.

Dr. Molly Wagster
301-496-9350, Fax: (301)496-1494
Email: wagsterm@mail.nih.gov

K. Development of technology and analysis tools to examine, in a systematic way, genetic, epigenetic, transcriptomic, metabolomic, and cell stress pathways in neurons and glia of the aging brain. Development of molecular imaging technology for the *in vitro* and *in vivo* analysis of gene, epigenome, proteostasis and metabolic function in the normal aging brain and in the diseased aging nervous system.

L. Improved technology for the analysis of structural and functional brain connectivity at the cell, neural circuitry and global network levels to define the normal trajectory of brain structure and function over the adult lifespan. Development of technology, including non-invasive methods and novel probes, to monitor and manipulate the plasticity of neural circuits in the adult and aged nervous system. Development of novel markers of neural stem cell function (proliferation, migration, and

differentiation) as well as methods to assess the integration and function of stem cells in the nervous system.

Dr. Bradley Wise (neurobiology of brain aging)
301-496-9350, Fax: 301-496-1494
Email: wiseb@nia.nih.gov

or

Dr. Suzana Petanceska (MCI, AD, & other dementias of aging)
301-496-9350; Fax: 301-496-1494
Email: petanceskas@nia.nih.gov

or

Dr. Larry Refolo (Alzheimer's disease & other dementias of aging)
301-496-9350, Fax: 301-496-1494
Email: refolol@mail.nih.gov

M. Novel approaches for analysis of next-generation sequence data.

Dr. Marilyn M. Miller
301-496-9350, Fax: 301-496-1494
Email: millermr@mail.nih.gov

Division of Geriatrics and Clinical Gerontology (DGCG)

DGCG supports clinical and translational research on health and disease in the aged and research on aging over the human life span and its relationships to health outcomes. Translational research is of interest for developing and testing the effectiveness of interventions known to be efficacious for everyday clinical practice and health decision making. 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. 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.

B. Development of clinical decision support tools that help physicians caring for patients with multiple chronic conditions to prioritize the interventions that are most beneficial and relevant within the context of these patients' lives; or tools for patient self-management of multiple chronic conditions.

C. Devices and/or techniques for preventing or treating urinary incontinence.

D. Development of improved post-surgical treatments/technologies promoting wound healing, prevention of chronic wounds, or reduced scar formation.

Dr. Marcel Salive
301-496-6761, Fax: 301-402-1784
Email: saliveme@nia.nih.gov

E. 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.

F. 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.

G. 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.

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

Dr. Chhanda Dutta
301-435-3048, Fax: 301-402-1784
Email: cd23z@nih.gov

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

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

Dr. Chhanda Dutta
301-435-3048, Fax: 301-402-1784
Email: cd23z@nih.gov

J. Measuring ambulation and assessing factors contributing to problems in and/or related to ambulation and mobility in general

1. Development of improved instrumentation for biomechanical assessment of ambulation and falls.

2. Development of improved instrumentation to assess balance, sway, gait, and postural control to identify stable and unstable patterns of movement during activities of daily living

3. Development of improved quantitative methods of assessing postural perturbations relevant to activities of daily living.

K. Development of improved, lightweight, and absorbent materials or other interventions to prevent, protect against and minimize injuries suffered from falls.

L. Development of assistive technologies to enable and support older persons to live independently and safely at home

   1. Development of devices/assistive technologies addressing complications of limited mobility among older persons.

M. Development of technologies to assist in the improvement of physical function and mobility in older persons prior to (prehabilitation) or following (rehabilitation) elective/planned surgery.

N. Research on better ways to prevent injuries and deaths associated with the use of currently-available bed rails in populations of older patients. Such research would include work on their identification and testing of improved designs of bed systems for use in homes, skilled nursing facilities, and hospitals.

Dr. Lyndon Joseph
301-496-6761; Fax: 301-402-1784
Email: Lyndon.Joseph@nih.hhs.gov

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

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

Ms. Winifred Rossi, M.A.
301-496-3836, Fax: 301-402-1784
Email: wr33a@nih.gov

Q. Development and validation of improved approaches for evaluation, monitoring or treatment of diastolic dysfunction in older adults.

R. Development and validation of improved techniques for hemodynamic monitoring of older adults in emergency and/or critical care settings.

S. Development and validation of instruments or methods to evaluate fatiguability—the level of fatigue related to the intensity, duration, and/or frequency of activity (in contrast to measures of fatigue), particularly in adults with or at-risk of developing age-related conditions or diseases leading to physical disability.

T. Development and validation of innovative approaches to pain control that consider age-related physiologic changes such as gastrointestinal absorption, cutaneous integrity, and musculoskeletal structure and function.

U. Development and evaluation of treatment approaches to age-related diseases or conditions based on modulation of the thyroid hormone axis.

V. Interventions and methods for screening, diagnosis, and treatment of cancer in older persons.

W. Development of methods to accurately determine the renal glomerular filtration rate (GFR) in older persons and patients with chronic kidney disease. The new methods should justify the effects of age-related changes in muscle mass, levels of serum creatinine, renal blood flow and renal concentrating ability.

X. Identification of novel biomarkers of acute kidney injury and chronic kidney disease in older persons. Such research would include identification of biomarkers and evaluation of their clinical utility for early diagnosis, prediction of the course of progression of diseases and/or monitoring the effects of treatment.

Y. Development and validation of new technology such as non-invasive methods to examine blood-flow velocity in arteries, individual coronary arteries, renal arteries, and cerebral arteries.

Dr. Basil A. Eldadah
301-496-6771; Fax: 301-402-1784
Email: eldadahb@nia.nih.gov

For additional information on research topics and administrative questions, contact:

Dr. Michael-David ("M-D") A.R.R. Kerns
Health Scientist Administrator
National Institute on Aging
Gateway Building, Suite 2C218
7201 Wisconsin Ave., MSC 9205
Bethesda, MD 20892-9205
301-402-7713, Fax: 301-402-2945
Email: michael-david.kerns@nih.hhs.gov

For budget management questions, contact:

Ms. Linda Whipp
Grants Management Officer
National Institute on Aging
Gateway Building, Room 2N212
7201 Wisconsin Ave., MSC 9205
Bethesda, MD 20892
301-496-1472, Fax: 301-402-3672
Email: lw17m@nih.gov

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

NIAAA supports research on the causes, prevention, control, and treatment of the major health problems associated with alcohol use. Through its extramural research programs, 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. NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

In addition to Phase I studies in the pursuit of the above aims, NIAAA will also accept Phase II and Phase IIB applications. For additional information about areas of interest to the NIAAA, you are invited to visit our home page at http://www.niaaa.nih.gov.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NIAAA may decrease the length of an award and/or the budget recommended by a review committee, or not fund an application. NIAAA will make awards compliant with all statutory guidelines as outline above. Total funding support (direct costs, indirect costs, fee) normally may not exceed $150,000 for 6 months for Phase I awards and $1,000,000 for up to two years for Phase II awards. With appropriate justification from the applicant, NIAAA may consider awards that exceed these amounts by up to 50% ($225,000 for Phase I and $1,500,000 for Phase II, a hard cap). Applicants considering a requested budget greater than the standard limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB Competing Renewal Awards

NIAAA will accept SBIR/STTR Phase IIB 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, 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.

Please contact Dr. Kathy Jung (contact information provided below) before beginning the process of putting an application together. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Phase IIb 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-12-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 Phase IIB Competing Renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase IIB 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:

Kathy Jung, Ph.D.
Phone: 301-443-8744
Fax: 301-594-0673
Email: Kathy.Jung@nih.gov

Pharmaceutical Development for Alcoholism Treatment

The topic focuses on 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 drugs capable of improving or reversing alcohol-induced cognitive impairments

C. Development of agents to treat associated psychiatric disorders and/or drug abuse, and to diminish drinking

D. 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.

E. Development of drugs for the treatment of alcoholic hepatitis, liver fibrosis, cirrhosis, pancreatitis, cardiomyopathy, or other alcohol-induced tissue damage

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

For clinical questions, contact:

Joanne B. Fertig, Ph.D.
301-443-0635
Email: Joanne.Fertig@nih.gov

For pre-clinical questions, contact:

Mark Egli, Ph.D. (Neuroscience and behavior)
301-594-6382
Email: Mark.Egli@nih.gov

Svetlana Radaeva, Ph.D. (Organ damage)
301-433-1189
Email: Svetlana.Radaeva@nih.gov

Diagnostic Assessment of Alcohol Use Disorders and Comorbidity

Innovative self-report and biochemical approaches to the early identification 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 of innovative methods for diagnostic assessment in clinical settings. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.

Megan Ryan, MBA
301-443-4225
Email: mryan1@mail.nih.gov

Treatment of Alcoholism

A. Development and evaluation of innovative therapeutic approaches across the continuum of alcoholism care.

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

C. Development and validation of efficacious computerized behavioral interventions for use in reaching remote or underserved populations of problem drinkers.

Megan Ryan, MBA
301-443-4225
Email: mryan1@mail.nih.gov

Technological Methods

Develop and validate ecological momentary assessment (EMA) methods (e.g., interactive voice response technology, cell phones, and transdermal alcohol monitors) for capturing real-time data for use in clinical trials and treatment paradigms.

Devise novel methods (e.g., Web-mining software of social networking sites) that capture social network information among groups at risk for alcohol dependence and high-risk drinking.

Daniel Falk, Ph.D.
301-443-0788
falkde@mail.nih.gov

Prevention

This area of interest focuses on the development and evaluation of innovative prevention and 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 intervene with the elderly around 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 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.

Robert C. Freeman, Ph.D.
301-443-8820
Email: Robert.Freeman@nih.gov

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 and assessment of protocols to assist in the identification, recruitment, and selection of treatment personnel to enhance the matching of staff to program needs.

B. Development and assessment 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.

C. Development and assessment of software to assist clinicians in scoring and assessment of score norms for commonly used assessment instruments. These packages should include protocols for guiding client feedback in a clinic or office-based setting.

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

E. Development and assessment of protocols to facilitate the selection, implementation, adoption, and maintenance of evidence-based services consistent with target population need, staffing and program resources, and expected outcomes. These protocols should be flexible enough to work across a variety of settings and modalities.

F. Development and assessment 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/or other health care settings. Research projects should facilitate the provisions of brief interventions, medical management, effective referral to specialized alcohol treatment, and follow-up.

G. Development and assessment of software or other protocols for monitoring service costs of alcohol treatment services including core, ancillary, out-sourced 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: Bob.Huebner@nih.gov

Fetal Alcohol Spectrum Disorder (FASD) and Alcohol-Related Birth Defects

FASD is the collective term for the broad array of adverse effects resulting from in utero alcohol exposure. The most severe of these is fetal alcohol syndrome (FAS), a developmental disorder characterized by craniofacial abnormalities, growth retardation, and nervous system impairments that often include mental retardation. Other diagnostic categories include partial FAS, alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD). Children and adults with FASD may exhibit multiple cognitive, behavioral, and emotional deficits that impair daily functioning in many domains. The NIAAA supports research leading to improved diagnosis and assessment of prenatal exposure, impairment and

disability, as well as the development of therapeutic interventions, including 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 and assessment of diagnostic and/or screening methods, tools or technology that can be used prenatally to identify fetuses affected by ethanol.

B. Development and validation of biomarkers that can be used to verify prenatal alcohol exposure in neonates.

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

D. Development and testing of skill-building, therapeutic, and education program products that enhance the social, cognitive, adaptive and motor abilities of individuals with FASD.

E. Development of neurobehavioral tools or instruments to assess responsiveness of individuals with FASD to medications and/or cognitive/behavioral therapies.

F. 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.

G. 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.

H. Development and validation of innovative methods, tools or technology to prevent harmful drinking during pregnancy.

For basic research questions, contact:

Dale Hereld, MD, Ph.D.
301-443-0912
Email: Dale.Hereld@nih.gov

William C. Dunty, Ph.D.
301-443-7351
Email: William.Dunty@nih.gov

For prevention research questions, contact:

Marcia Scott, Ph.D.
301-402-6328
Email: Marcia.Scott@nih.gov

Alcohol Use and HBV or HIV Infection or Co-infection

Alcohol Use and HBV or HIV Infection or Co-infection Alcohol use, including hazardous drinking, by persons infected with HIV and HBV is quite common in the United States. Alcohol consumption is widely acknowledged as a co-factor in the sexual transmission, susceptibility to infection, and progression of the infectious diseases. However, detailed relationships between alcohol use and viral infections, diseases progression, antiretroviral therapy and adverse outcomes, notably in liver disease progression, are less recognized or understood. Recent research indicates that inflammatory pathways predominate in alcoholic hepatitis whereas adaptive immunity plays a primary role in viral hepatitis, offering multiple targets for novel preventive and therapeutic interventions. Comprehensive studies to improve understanding of the factors underlying alcohol and viral etiologies in liver disease and the impact of antiretroviral drugs on liver disease progression are needed. A better understanding of alcohol's effects on liver disease in patients with HIV and HBV infection or co-infection may improve diagnosis and

treatment outcomes. NIAAA supports research leading to improved diagnosis and treatment of alcohol-induced disorders in people infected with HIV and HBV, or both.

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

A. New preventive and therapeutic approaches designed to protect the liver from alcohol and antiretroviral drug-induced liver injury in patients infected with HIV and HBV mono- or co-infection.

B. Development of therapies aimed at molecular targets that play a role in the development of alcoholic and viral liver diseases.

C. Develop and evaluate drugs that mitigate the effects of oxidative stress on mitochondrial function thereby preventing liver disease progression.

D. Development of biomarkers for individuals who are most prone to alcohol-induced damage in those patients infected with HIV and HBV mono- or co-infection.

For HBV and basic research questions on HIV, contact:

H. Joe Wang, Ph.D.
301-451-0747
Email: He.Wang@nih.gov

For clinical or epidemiological questions on HIV, contact:

Kendall J. Bryant, Ph.D.
301-402-9389
Email: Kendall.Bryant@nih.gov

Development of Biomolecular Signatures of Alcohol Exposure and Alcohol-induced Tissue Injury

Acute and chronic alcohol consumption leads to health-related complications and ultimately to significant societal costs. Quantitative and qualitative markers of high-risk drinking behavior and alcohol-induced tissue damage would greatly improve medical efforts to recognize and treat alcohol-related disorders. Traditional biomarkers currently in clinical use lack specificity, sensitivity, and accuracy, and fail to provide long-term information. Biomarkers of sufficient reliability, sensitivity and specificity are likely to be comprised of a panel of physiological parameters, rather than a single molecular entity. Thus, NIAAA seeks to support the discovery and development of pattern-based molecular fingerprints or signatures of alcohol consumption and of alcohol-induced tissue injury. High throughput approaches using genomics, epigenomics, transcriptomics, proteomics, metabolomics, lipomics, or glycomics are encouraged. Biomarker signatures may be composed of multiple genes, RNAs, microRNAs, proteins, or metabolites, or combinations thereof. Furthermore, alterations in lipid, lipoprotein, or glycoprotein profiles may reflect the metabolic effects of alcohol exposure and may be considered as potentially predictive. Biomarker signatures that address multiple aspects of alcohol consumption and alcohol damage are needed. These include, but are not limited to:

A. Biomarkers of long-term alcohol consumption. A biomarker panel reflecting the cumulative intake of alcohol over a period of months or more would be of great diagnostic use, both in terms of recognizing problem drinking and in terms of the potential for organ damage.

B. Biomarkers that distinguish between binge, acute, moderate and chronic drinking. Each of these modes of alcohol intake has different physiological effects. The ability to distinguish dose and timing of drinking would enhance clinicians' ability to design appropriate treatment and intervention protocols.

C. Biomarkers of compliance after withdrawal. Biomarker signatures in this class would be comprised of metabolic products that decrease rapidly upon abstinence, in contrast to the characteristics of

biomarkers that reflect cumulative alcohol. The ability to detect relapse accurately will support successful behavioral interventions.

D. Biomarker signatures of alcohol-induced organ damage. The damage due to alcohol consumption is likely to be organ-specific, with signatures reflecting alcohol-induced damage likely to be different for heart damage, liver damage, encephalopathy, a dysregulated immune system, or other alcohol target.

E. Biomarker signatures of familial risk factors for alcoholism. Early identification of subjects predisposed to alcoholism will allow for early intervention, and allow subjects to make informed decisions.

P.J. Brooks, Ph.D.
301-402-0883
Email: PJ.Brooks@nih.gov

Alcohol Biosensors and Data Analysis Systems

It is anticipated that innovative and improved alcohol sensors would be useful in a variety of situations including, but not limited to, clinical monitoring, forensics and human or animal research. Specific sensor characteristics would complement their intended use. This applies to characteristics such as sampling frequency, degree of accuracy, data storage capacity and data transmission frequency.

Depending on their intended purpose and use, alcohol sensors may be augmented with additional information such as other physiological measurements or geospatial determinations. Devices need to be compatible with human comfort, and devices to be worn for weeks or months may present particular challenges. Since alcohol readings are likely to be baseline most of the time, these sensing devices generally require ways to monitor contact and readiness to record. Moreover, where necessary, measurement fidelity should be robust to subject's activities including active efforts at tampering.

The mode of data storage will need to conform to power limitations and strategies for data transmission which may require telemetry.

In addition to alcohol monitoring and data transmission this program also includes the opportunity to develop appropriate data analysis systems. Examples include: estimating blood alcohol concentrations, reconstructing patterns of alcohol consumption, and monitoring large numbers of devices to identify significant, but infrequent, events while minimizing false positives.

P.J. Brooks, Ph.D.
301-402-0883
Email: PJ.Brooks@nih.gov

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-glutamyl 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.

Raye Z. Litten, Ph.D.
301-443-0636
Email: Raye.Litten@nih.gov

Stem Cell Research for Alcohol-induced Disorders

Stem cells are master cells in the body and they have the remarkable potential to develop into many different cell types. Stem cells may become a renewable source of replacement cells to treat alcohol related diseases. They can also be used to study disease processes, and to develop new and more effective drugs.

Recent research progress on stem cells has offered great opportunities to study conditions and diseases related to alcohol abuse and alcoholism. Stem cells can come from embryos or adult tissues. They are generally categorized into 1) Embryonic stem cells; 2) Induced pluripotent stem cells (iPS cells); and 3) Adult stem cells. The NIAAA supports SBIR/STTR research using any of these 3 types of stem cell, which can lead to improved understanding of alcohol related diseases and conditions, and better treatment.

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

A. Generate and disseminate induced pluripotent stem cells (iPS) from mature human cells to resemble diverse individual variations regarding alcohol metabolism. Use these genetic variant models to study alcohol dependence and pharmacotherapy development. Examples of these genetic variations include Alcohol Dehydrogenase (ADH), Aldehyde Dehydrogenase (ALDH), cytochrome P450 isozyme CYP2E1, and Glutathione S transferase (GST).

B. Generate and disseminate disease-specific iPS cell lines for studies on the biology and signaling pathways that contribute to the alcohol-related disease pathology.

C. Models derived from human iPS cells to study biological and pathological effects of alcohol and its metabolites.

Peter Gao, M.D.
301-443-6106
Email: Peter.Gao@nih.gov

Role of non-coding RNAs in the Neuroadaptation to Alcoholism

Gene expression changes after alcohol exposure are well documented. In particular, a vast network of expression changes is found in the brain (and other tissues) following both acute and chronic alcohol exposure. These neuroadaptations are thought to underlie tolerance and dependence on alcohol as well as mediating the toxic effects of alcohol on neurodevelopment. The discovery of gene expression regulation mediated by RNA molecules that are transcribed from DNA but do not code for protein, has set into motion a revolution in molecular biology These novel RNAs are classified broadly as non-coding RNAs (ncRNAs) and include both small (microRNAs or miRNAs) and large classes (long non-coding RNAs or lncRNAs) that function to alter the expression of genes to which they bind and modify chromatin states. Because it is estimated that the majority of the genome consists of non-protein coding regions, of which ncRNAs make up a substantial portion, understanding how alcohol alters the expression of ncRNAs and their targets has significant potential for understanding the mechanisms of alcohol neuroadaptation. However, because of their diverse role in cellular functions and combinatorial mechanisms of action, many challenges still exist in gaining a full appreciation of the role of ncRNAs in alcohol neuroadaptation.

NIAAA seeks the development of novel technologies to both measure and interpret ncRNA gene expression signatures in the brain and/or primary neuronal cultures following alcohol exposure. These technologies could include, but are not limited to: novel methods to tag and measure ncRNAs, new imagining techniques to monitor changes in ncRNAs, and novel bioinformatic algorithms to interpret alcohol-induced alterations in ncRNAs and predict and validate target genes.

Matthew Reilly, Ph.D.
301-594-62228
Email: reillymt@mail.nih.gov

***In vivo* detection of neuromodulators in behaving animals**

Neuromodulators, such as neuroimmune factors, modulate a wide range of brain functions and play an important role in neurodevelopment and synaptic function. To understand how activities of neuromodulators contribute to alcohol use disorders and how changes at the molecular level link to behavior, effective tools are needed to detect changes of neuromodulators in real time in the brain of behaving animals. Currently available methods that measure neuromodulator levels in the CSF fluid would not allow the analysis of dynamic changes of neuromodulators with spatial and temporal precision. To facilitate the understanding of how neuromodulators shape neuronal activity and contribute to alcohol use disorders, more accurate methods of detection are needed.

Recent advances in a variety of *in vivo* neurotechniques provide a great opportunity to achieve this goal. For example, cell-based fluorescent reporters, which detect the activity of G protein-coupled receptors

through a fluorescent Ca2+ sensor, can be developed to detect neuromodulators that activate G protein-coupled receptors, such as chemokines. In addition, *in vivo* fluorescence imaging using target-activated small-molecule fluorochromes coupled with nanotechnology may also provide a powerful tool to visualize neuromodulator changes in the intact brain.

With this SBIR/STTR solicitation, NIAAA seeks the development and application of techniques that can detect neuromodulator changes in real time with spatial and temporal precision in behaving animals. Techniques that allow the *in vivo* detection of neuromodulators over an extended time period, such as implantable cell- or probe-based biosensors, will be particularly encouraged.

Changhai Cui, Ph.D.
301-443-1678
Email: Changhai.Cui@nih.gov

Ex vivo Efficacy Screens to Identify Pharmacotherapies for Alcohol Dependence

High throughput screening efforts have identified many small molecules acting at biological targets thought to be important modulators of excessive alcohol drinking and other alcohol dependence phenotypes. Concurrently, *in vivo* animal models of alcohol drinking and related behavioral measures are currently used to assess potential therapeutic efficacy of medications under development. *Ex vivo* efficacy screens are an important link between these two activities. In contrast to many behavioral models, *ex vivo* tissue-based assays are desirable for their simplicity, speed, and capacity to test small drug quantities. To date little attention has been devoted toward developing and validating neuronal tissue and cell based screening platforms that can be used to inform go/no go decisions for subsequent *in vivo* preclinical efficacy testing.

With this SBIR/STTR grant solicitation, NIAAA seeks the development and validation of *ex vivo* screens capable of predicting efficacy test results in preclinical behavioral models of alcohol dependence. Such assays may include arrays of parameters capable of differentiating the alcohol dependant from the non-dependent state. They should also discriminate positive and negative control drugs found in the alcohol dependence pharmacotherapy literature and be sensitive to drugs with diverse mechanisms of action. In addition, the assays developed under this solicitation should be relatively rapid, simple and produce consistent and reliable results in multiple laboratories.

Mark Egli, Ph.D.
301-594-6382
Email: Mark.Egli@nih.gov

Changhai Cui, Ph.D.
301-443-1678
Email: Changhai.Cui@nih.gov

Develop Network Pharmacology Strategy for Preclinical Medication Development

The frequent failure of using highly selective drugs for disease treatment has challenged the concept of “one gene, one drug and one disease” and led to the emergence of a new paradigm, network pharmacology, as a drug development and treatment strategy. This strategy combines the knowledge of biological networks with multiple drug targets to simultaneously regulate multiple pathways perturbed by disease conditions. Given the multi-target nature of alcohol action, alcoholism arises from brain network perturbation. The network pharmacology/combined pharmacological approach, either using drug combinations or multi-target drugs, may serve as an effective strategy for the treatment of alcohol-induced brain dysfunction and behavior disorders.

NIAAA seeks preclinical development of combined pharmacological approaches to synergistically regulate multiple drug targets for alcoholism. Areas that may be of interest to small businesses include, but are not limited to:

Objective 1: Develop and validate new target combinations using cellular and animal models.

Objective 2: Prioritize multi-drug targets and identify the effective drug combinations or multi-target drugs for the medication development.

Objective 3: Use high-throughput screening of compound libraries to identify multi-target drugs.

Objective 4: Encourage adaption of low throughput assays to high throughput screening, development of lead compounds, and identification of drug candidate(s) with proper pharmaceutical properties for medication development.

Changhai Cui, Ph.D.
301-443-1678
Email: Changhai.Cui@nih.gov

Novel tools and technologies to detect the effects of alcohol on the CNS structure and activities

Alcohol affects virtually all of the major neurotransmission systems in the brain by interacting with membrane ion channels, neurotransmitter release machineries and receptors, signal transduction pathways, genes and epigenetic factors. In order to better understand the acute and chronic effects of alcohol and mechanisms of alcohol intoxication and dependence, it's important to be able to simultaneously detect the structure and activities of large numbers of neurons with intact connections to facilitate the analysis of neurocircuits. Equally important, structure and activities in different subcellular domains (soma, dendrites, spines, axon, etc.) of CNS neurons need to be monitored with high temporal resolution. Additionally, recent developments indicate that glial cells play more important roles in the normal function of the brain and may be important alcohol targets. There is a need to monitor glia-neuron interactions.

There have been great advances in recent years in chemical and optogenetic methodologies, enabling improved ability to monitor CNS structure and activities in larger numbers and at much higher spatial and temporal resolution. Building upon these advances, NIAAA seeks SBIR/STTR research to develop the novel tools and technologies to detect the effects of alcohol on activities of specific cell types, neuron-glia interactions, and the structure and activities of large numbers of neurons in alcohol-drinking/exposure settings, preferentially with intact neural network. These will include, but not limited to, the following:

- Improving chemical or genetic sensors to detect dynamic changes in calcium, voltage, cAMP etc.
- Developing tools and sensors to monitor structure and activities of neurons and glial cells, and their interactions
- Developing tools and sensors to monitor synaptic activities
- Defining cell types in the neurocircuits
- Developing miniature and nanoscale apparatus and sensors, or miniaturizing and optimizing detection apparatus for the study of alcohol effects
- Developing computational methods for the acquisition and analysis of large scale data

Qi-Ying Liu, M.D., M.Sci.
301-443-2678
Email: liuqiy@mail.nih.gov

Changhai Cui, Ph.D.
301-443-1678
Email: changhai.cui@nih.gov

Lindsey Grandison, Ph.D.
301-443-0606
Email: lgrandis@mail.nih.gov

Research Tools

The NIAAA supports the development of new or improved tools to enhance the ability to conduct alcohol-related laboratory studies on humans and animals and to more effectively analyze data from large databases. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of novel 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 specialized cell culture chambers to provide controlled administration of ethanol to *in vitro* cell systems.

D. Development of experimental systems that mimic organ function, including, but not limited to, co-culture and novel approaches to three dimensional culture.

E. Development of new methods of ethanol administration to animals that produce precise dose control or that closely mimic types of alcohol exposure occurring in humans, including, but not limited to, binge drinking, acute consumption, moderate consumption and chronic consumption.

F. Development of ligands which will enhance the potential usefulness of PET and SPECT neuroimaging technologies for the study of the etiology of alcoholism and related brain pathology.

G. Development of computational, statistical or bioinformatics tools to organize and manage high throughput data obtained by genomic, functional genomic or other ‘omic strategies.

H. Development of databases, methods for integration of databases, or data analysis systems for alcohol research.

Kathy Jung, Ph.D.
301-443-8744
Email: Kathy.Jung@nih.gov

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

For additional information on research topics, contact:

Kathy Jung, Ph.D.
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane, Room 2021
Bethesda, MD 20892-9304
For Federal Express delivery, use:
Rockville, MD 20852-1705
Phone: 301-443-8744
Email: Kathy.Jung@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: Judy.Fox@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 Programs, please visit http://www.niaid.nih.gov/researchfunding/sb/pages/default.aspx.

Limited Total Amounts for Phase I and Phase II Awards

Congress raised the "normal" SBIR and STTR awards to $150,000 for Phase I and $1 million for Phase II (total costs for all years of an award). With appropriate applicant justification, Congress allowed awards to exceed these amounts, but only by 50%, i.e., up to $225,000 for Phase I and $1.5 million for Phase II (budget caps). For topics listed in APPENDIX A: National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations the NIAID will consider issuing an award exceeding these hard caps based on availability of funds and programmatic needs. Applicants are strongly encouraged to contact NIAID program officials prior to submitting any application in excess of the guidelines. In all cases, applicants should propose a budget that is reasonable and appropriate for completion of the research project.

Phase IIB SBIR Competing Renewal Awards

The NIAID will accept Phase IIB SBIR Competing Renewal grant applications to continue the process of developing products that require approval of a 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/researchfunding/sb/pages/sbirareas.aspx). NIAID will not accept Phase IIB STTR Competing Renewal applications.

NIAID will accept Phase IIB SBIR Competing Renewal applications for a project period of two years and a budget not to exceed a total cost of $1.5 million for the total Phase IIB award (including direct cost, F&A, and fee/profit).

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. NIAID SBIR Phase IIB Competing Renewal grant applications may exceed this guideline, however, when well justified and when those costs are necessary to support preclinical studies 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, and subcontracts to assure compliance with Good Manufacturing Practices expectations of the FDA.

Human clinical trials may not be a component of proposed SBIR or STTR research. See Notice of NIAID Policy on investigator initiated clinical trials at http://grants.nih.gov/grants/guide/notice-files/NOT-AI-10-

024.html. Small business applicants are encouraged to contact relevant program officers (below) to discuss NIAID funding for human clinical trials.

NIAID does NOT request a letter of intent for Phase IIB Competing Renewal Applications. For more information about NIAID small business awards, please visit our web page:

http://www.niaid.nih.gov/researchfunding/sb/Pages/default.aspx

You can also contact a program officer listed below within a relevant area of interest.

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. Carl Dieffenbach
301-496-0545
Email: cd17u@nih.gov

BASIC SCIENCES PROGRAM

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

Contact: Dr. Diana Finzi
301.451.2598
Email: Dfinzi@niaid.nih.gov

A. ***Epidemiology Branch.*** Population-based research, modeling, and comparative effectiveness studies (not including clinical trials) that assess the natural history, biologic, and clinical course of HIV/AIDS, and related outcomes, and could advance treatment and prevention of HIV. Specific interests include factors related to HIV transmission and associated biological and behavioral factors, basic research on immunology, virology, and antiretroviral therapy, issues surrounding care for HIV and other co-morbidities, interactions and impact on clinical outcomes. Development of novel electronic tools, including devices and computer programs to enhance behaviors such as treatment adherence or uptake of treatment guidelines, is also of interest.

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

B. ***Basic Research Branch.*** Identification and characterization of potential targets for discovery or design of novel strategies to impact HIV transmission, virus-host interactions, host restriction factors, chronic immune activation, and HIV latency/persistence. Innovative approaches for monitoring or studying HIV infection, immunopathogenesis, and viral reservoirs that persist despite antiretroviral therapy. Development of assays and technologies involving nanotechnology and single-cell analysis is of particular interest.

Contact: Dr. Karl Salzwedel
301-496-5332
Email: salzwedelkd@niaid.nih.gov

C. ***Targeted Interventions Branch.*** Identification of small molecule inhibitors, using standard and high-throughput technologies, with novel or underexplored mechanisms of action; gene therapies; RNA-based therapeutics; novel targeting and delivery vehicles for agents active against HIV; therapeutic

vaccines, monoclonal antibodies, and immune-based therapies; assays to quantitate latent virus; animal models to facilitate evaluation of agents to treat or cure HIV infection

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

VACCINE RESEARCH PROGRAM

Supports the discovery, development and clinical evaluation of an HIV/AIDS vaccine.

Director: Dr. Mary Marovich
301.435.3727
Email: mary.marovich@nih.gov

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

Contact: Dr. Thandi Onami
301-594-1321
Email: Thandi.onami@nih.gov

B. ***Preclinical Research and Development Branch.*** Preclinical development of candidate AIDS vaccines, delivery methods, novel vaccine vectors, 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 studies 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: yli@niaid.nih.gov

C. ***Vaccine Translational Research Branch (VTRB).*** Translational research to facilitate advancing novel promising basic SIV/HIV vaccine research concepts into HIV vaccine products that can be evaluated in human clinical trials. Research areas encompassed in translational research involve: (1) vector optimization for expression, safety, and manufacturability; (2) upstream and downstream development activities; (3) analytics development to support in process testing and release; (4) formulation development; (5) novel adjuvant approaches; (6) GMP manufacturing; and (7) preclinical safety and toxicology modeling.

Contact: Dr. Michael Pensiero
301-435-3749
Email: mpensiero@niaid.nih.gov

THERAPEUTICS RESEARCH PROGRAM

Develops and oversees research and development of therapies for HIV disease, including complications, co-infections and co-morbidities, in adults.

Director: Dr. Sarah Read
301-451-2757
Email: readsa@niaid.nih.gov

A. ***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 anti-opportunistic infection compounds; immunologic, virologic, and pharmacologic research related to the design and conduct of clinical trials.

Chief: Dr. Mike Ussery
301-402-0134
Email: mussery@niaid.nih.gov

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

Contact: Tia Morton
301-435-3763
Email: frazierti@niaid.nih.gov

C. ***Complications & Co-Infections Research Branch.*** Preclinical and clinical research to develop new or improved therapies for the treatment and prophylaxis of Pneumocystis Pneumonia, Mycobacterium avium Complex, and cryptococcal disease.

Contact: Dr. Chris Lambros
301-435-3769
Email: clambros@niaid.nih.gov

D. ***For evaluation of therapeutic agents or diagnostics for hepatitis B or hepatitis C secondary to HIV infection in adults.***

Contact: Dr. Susan Brobst
301-435-3762
Email: sbrobst@niaid.nih.gov

E. ***Tuberculosis Clinical Research Branch.*** Translational and clinical research for tuberculosis, with and without HIV co-infection, to facilitate the development of biomarkers/diagnostics, therapies, and prevention/vaccines.

Contact: Sharon D. Williams
301-451-2616
Email: SW386Z@nih.gov

PREVENTION SCIENCE PROGRAM

Supports basic research on mechanisms of HIV transmission supportive of new biomedical strategies for interrupting transmission. 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.

Acting Director: Sheryl Zwerski, MSN, CRNP
301-402-4032
Email: szwerski@niaid.nih.gov

A. ***Preclinical Microbicides and Prevention Research Branch.*** Preclinical pipeline for non-vaccine biomedical prevention products including topical microbicides, pre-exposure prophylaxis (PrEP) and multipurpose prevention technologies (MPT). Iterative approaches of existing and emerging technologies into a translational pipeline to select and advance the most promising candidates to clinical evaluation.

Chief: Dr. Jim Turpin
301-451-2732

Email: jturpin@niaid.nih.gov

B. ***Clinical Microbicide Research Branch.*** Clinical development of promising microbicides to prevent HIV infection with the ultimate goal to advance safe, effective and acceptable microbicide products toward licensure.

Chief: Dr. Roberta Black
301-496-8199
Email: rblack@niaid.nih.gov

C. ***Clinical Prevention Research Branch.*** Development of safe and effective non- vaccine biomedical and integrated HIV prevention interventions to reduce the number of new HIV infections in adults and adolescents. Support the development of HIV incidence assays, biomarkers of adherence, and mathematical modeling.

Chief: Dr. David Burns
301-435-8896
Email: burnsda@niaid.nih.gov

D. ***Maternal, Adolescent and Pediatric Medicine Branch.*** Therapies for cure, management, treatment and prevention of HIV and HIV associated complications in pregnant women, infants, children and adolescents. Strategies to reduce transmission of HIV and HIV co-infections from mother to child.

Contact: Judi Miller, R.N.
301-496-1189

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. ***Allergy, Asthma and Airway Biology Branch.*** Conditions of interest: asthma, food allergy, eosinophilic esophagitis and gastroenteritis in relation to food allergy, atopic dermatitis, urticaria, rhinitis, rhinosinusitis, drug allergy, sepsis. The Branch supports basic and clinical studies investigating mechanisms of disease and new approaches to diagnose, treat or prevent these conditions. Special interest for SBIR/STTR includes the development of methodologies to manage, and analyze clinical and epidemiologic research in the above conditions and the development of biomarkers as diagnostic markers, markers of disease severity, predictive markers for treatment effectiveness, particularly of immunologic interventions such as allergen immunotherapy for food and respiratory allergy.

Chief: Alkis Togias, M.D.
301-496-8973
Email: togiasa@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, immune 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: 301-480-2381
Email: hquill@niaid.nih.gov

C. **Autoimmunity and Mucosal 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, and biomarkers, 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 Branch.*** Preclinical and clinical research in organ, vascularized composite tissue and cellular transplantation: acute and chronic graft rejection, allogeneic and xenogeneic transplantation, development of immunomodulatory agents to prevent and treat graft rejection and to promote acute and long term graft acceptance and immunologic tolerance, genomics of the alloimmune response, graft versus host disease and engraftment for hematopoietic stem cell transplantation, minor histocompatibility antigens, complications of immunosuppression in transplantation, and major histocompatibility complex (MHC) region genomics and technologies for MHC typing.

Chief: Nancy D. Bridges
301-496-5598
Email: nbridges@niaid.nih.gov

E. ***Radiation Countermeasures Program.*** Identification and evaluation of medical countermeasures (MCMs) for public health radiation emergencies through the development of mitigators and therapeutics for acute radiation syndrome or the delayed effects of acute radiation exposure; radionuclide-specific therapies, including chelating agents, blocking agents, and other novel decorporation agents; improved methods of accurate and high-throughput radiation biodosimetry and bioassays for radionuclide contamination; biomarkers of organ-specific radiation injury; therapeutics for radiation combined injury; therapeutics for radiation-induced immunosenescence; and formulations for pediatric administration.

Chief: Dr. Bert Maidment
301-594-0641
Email: maidmentb@niaid.nih.gov

Division of Microbiology and Infectious Diseases

The Division of Microbiology and Infectious Diseases (DMID) supports research to better understand, treat, and ultimately prevent infectious diseases caused by virtually all infectious agents, except HIV. DMID supports a broad spectrum of research from basic molecular structure, microbial physiology and pathogenesis, to the development of new and improved vaccines and therapeutics. 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 and emerging infectious disease research.

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

A. ***Bacteriology and Mycology Branch.***

The branch oversees research on medical mycology, hospital infections (including Acinetobacter, Klebsiella, Serratia, Legionella, Pseudomonas, Aeromonas, Enterobacter, Proteus, non-enteric E. coli, actinomycetes and others), staphylococci, enterococci, bacterial zoonoses (plague, anthrax, tularemia, glanders, melioidosis, Lyme disease, rickettsial diseases, anaplasmosis, ehrlichiosis and Q fever), and leptospirosis. Research is encouraged in the following general areas: (1) product vaccines, adjuvants, therapeutics and diagnostics (including target identification and characterization, device or apparatus development, novel delivery, and preclinical evaluation); (2) products to combat antibacterial and antifungal drug resistance; (3) applied proteomics and genomics; (4) host-pathogen interactions, including pathogenesis and host response; (5) genetics, molecular, and cell biology; and (6) microbial structure and function.

Research in the following areas is of particular interest to the branch, but research on all of the above is welcome:

- Vaccines, therapeutics, and medical diagnostics for hospital infections
- Adjunctive therapies and non-traditional approaches to combat antimicrobial resistance
- Diagnostics for invasive fungal disease
- Novel approaches for the diagnosis of Lyme disease

Contact: Dr. Alec Ritchie
301-402-8643, Fax: 301-402-2508
Email: aritchie@niaid.nih.gov

B. ***Enteric and Hepatic Diseases Branch.***

Special emphasis areas include vaccines against hepatitis C virus; antimicrobials and antivirals that focus on novel targets such as host-pathogen interactions to combat the development of resistance; vaccines and therapies for botulinum neurotoxins, especially therapies that that target toxins once they enter cells; therapies and diagnostics for *Clostridium difficile* that include recurrent disease issues; development of a simple, rapid point-of-care diagnostic tools for the simultaneous identification of multiple diarrheal pathogens that includes their antibiotic resistance profiles; diagnostics for use in low-resource settings, pediatric vaccines to prevent the major worldwide causes of diarrhea; more fieldable vaccines and improved formulation methods; and novel therapeutics for chronic hepatitis B and C.

Research areas of the Branch include the following organisms and diseases: astrovirus, *Bacteroides spp.*, *Campylobacter spp.*, enteric *Clostridia spp.* including botulinum neurotoxins, commensals and normal flora, pathogenic *Escherichia coli*, gastroduodenal disease, gastroenteritis, *Helicobacter spp.*, *Listeria spp.*, Noroviruses including Norwalk, ricin toxin, rotaviruses, *Salmonella* serovars, *Shigella spp.*, Staphylococcus enterotoxin B, *Vibrio spp.* enteric *Yersinia spp.*, hepatitis viruses A, B, C, D, and E, as well as cholera, diarrhea, enterotoxins, gastroenteritis, gastroduodenal disease and ulcers, and Guillain-Barre syndrome.

Program Contact: Dr. Rodolfo Alarcon
301-451-3022, Fax: 301-402-1456
Email: alarconrm@niaid.nih.gov

C. ***Parasitology and International Programs Branch.***

Research areas: (1) protozoan infections, including amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis; helminth infections, including cysticercosis, echinococcosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes); invertebrate vectors/ectoparasites, black flies, sandflies, tsetse flies, mosquitoes, ticks, snails, mites; (2) parasite biology (genetics, genomics, physiology, molecular biology, and biochemistry); (3) protective immunity, immunopathogenesis, evasion of host

responses; (4) clinical, epidemiologic, and natural history studies of parasitic diseases; (5) research and development of vaccines, drugs, immunotherapeutics, and medical diagnostics, and (6) vector biology and management; 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** caused by influenza viruses, human coronaviruses including SARS and novel emerging coronaviruses, rhinoviruses,respiratory syncytial virus and other related paramyxoviruses; (2) **mycobacterial diseases**, including tuberculosis, leprosy, Buruli ulcer and non-tuberculous mycobacterial diseases; (3) **other bacterial respiratory diseases** including acute otitis media, community acquired pneumonia, acute exacerbations of chronic obstructive pulmonary disease, diphtheria, pertussis, acute rhinosinusitis, streptococcal disease; and (4) **mixed viral/bacterial respiratory infections**.

Special emphasis areas: development of new or improved antimicrobials and antivirals, including immunotherapeutics, new or improved vaccines (with and without adjuvants), improved delivery systems for drugs/vaccines, biomarkers, rapid multiplex diagnostic tests, including low cost point-of-care, or other tools to detect infection prior to active disease and identify drug resistance. There is particular need for preventive and treatment countermeasures for influenza, including universal vaccine platforms and broad-spectrum antivirals, for tuberculosis (TB) diagnostics, including drug susceptibility tests and novel anti-TB vaccines and antimicrobials, and for new vaccines and improved treatment options for *Streptococcus pneumoniae*.

Contact: Gail Jacobs
301-496-5305, Fax: 301-496-8030
Email: ggjacobs@niaid.nih.gov

E. ***Sexually Transmitted Infections Branch.***

Areas of emphasis include the development of medical diagnostics including better and more rapid multiplex point of care tests, ability to rapidly determine antibiotic sensitivity, and novel technologies enabling testing in low resource settings while maintaining high sensitivity/specificity; development of new classes of antimicrobials and nonantimicrobial treatment approaches, particularly those focused on reducing the development of antibiotic resistance; novel delivery systems for microbicides, vaccines and therapeutics for Sexually Transmitted Infections (STIs) and other reproductive tract syndromes such as bacterial vaginosis and pelvic inflammatory disease; understanding vaginal ecology and immunology and approaches to developing synthetic microbiotia for use as biotherapeutics or as adjunct therapy to antibiotic treatment; development of epidemiologic and behavioral strategies to reduce transmission of STIs; developing and evaluating interventions and products to better serve adolescents, medically underserved populations, and minority groups who are disproportionately affected by STIs; development of multipurpose prevention technologies to prevent STIs, HIV, and unintended pregnancies; better understanding of the role of STIs in infertility, premature birth, and adverse outcomes of pregnancy and how to improve outcomes; and better understanding of the role of STIs in HIV transmission and the role of HIV in altering the natural history of STIs.

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

F. ***Virology Branch.***

Areas of emphasis for SBIR/STTR applications include:1) vaccine development; 2) development of therapeutic interventions or diagnostics; 3) development and validation of assays for disease

diagnosis and to measure response to therapy; 4) approaches to identify antiviral targets and agents; 5) chemical design and synthesis of novel antiviral agents; 6) development of new preclinical model systems that predict clinical efficacy of vaccines, therapeutics and diagnostics. The Virology Branch does not support applications covering environmental detection and decontamination.

The Virology Branch focuses on the following: acute viral infections (including Nipah and Hendra viruses), arthropod-borne and rodent-borne viral diseases (including Dengue, West Nile, Japanese encephalitis, Chikungunya, yellow fever, hantavirus, etc.), viral hemorrhagic fevers (Ebola, Lassa fever, etc.), measles, polio, coxsackie virus, enteroviruses, poxviruses, rabies, rubella,and . persistent viral diseases (including adenoviruses, BK virus, bornaviruses, coronaviruses, herpesviruses, human T-lymphotrophic virus, JC virus, human papillomaviruses, parvoviruses, emerging human polyomaviruses, and prion diseases).

Contact: Dr. Ramya Natarajan
301-594-1586, Fax: 301-402-0659
Email: ramya.natarajan@nih.gov

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

Please visit our Small Business High-Priority Areas of Interest:
http://www.niaid.nih.gov/researchfunding/sb/pages/sbirareas.aspx

For additional information about the NIAID SBIR/STTR program contact:

Dr. Natalia Kruchinin
SBIR/STTR Program Coordinator
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
301-4968666, Fax: 301-480-1993
Email: kruchininn@niaid.nih.gov

For administrative and business management questions, contact:

Mr. Michael Wright
Grants Management Specialist
National Institute of Allergy and Infectious Diseases
301-451-2688, Fax: 301-493-0597
Email: mawright@mail.nih.gov

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

The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases.

For additional information about areas of interest to the NIAMS, please visit NIAMS Long Range Plan at http://www.niams.nih.gov/About_Us/Mission_and_Purpose/long_range.asp.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NIAMS may decide not to fund an application or may decrease the length of an award and/or the budget recommended by a review committee. Generally,

NIAMS does not fund Phase I applications with a total cost greater than $225,000 or a project period greater than 2 years and Phase II applications with a total cost greater than $1,500,000 or a project period greater than 3 years. Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application. It is not the intent of NIAMS to support clinical trials through the SBIR/STTR mechanism. Applicants who wish to submit clinical trials applications to the NIAMS are encouraged to utilize one of the NIAMS FOAs listed HERE.

Arthritis and Musculoskeletal and Skin Diseases

A. ***Division of Skin and Rheumatic Diseases.*** This division promotes and supports: basic and clinical studies of the skin in normal and disease states; and research leading to prevention, diagnosis and cure of rheumatic and related diseases. In the area of Skin Diseases, the division has a wide range of skin diseases under study with NIAMS support, to include 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. In the area of Rheumatic Diseases, the division supports basic, epidemiologic, and clinical research on etiology, pathogenesis, course, interventions, and outcomes in rheumatic and related diseases.

   This is not an inclusive list of all research topics covered by the Division of Skin and Rheumatic Diseases. To learn more, please visit the Division page at http://www.niams.nih.gov/Funding/Funding_Opportunities/Supported_Scientific_Areas/Skin_Rheumatic_Diseases/default.asp.

B. ***Division of Musculoskeletal Diseases.*** The musculoskeletal system is composed of the skeleton, which provides mechanical support and determines shape; the muscles, which power movement; and connective tissues such as tendon and ligament, which hold the other components together. The cartilage surfaces of joints and the intervertebral discs of the spine allow for movement and flexibility.

   The Division of Musculoskeletal Diseases of the NIAMS supports research aimed at improving the diagnosis, treatment, and prevention of diseases and injuries of the musculoskeletal system and its component tissues. Key public health problems addressed by this research include osteoporosis, osteoarthritis, and muscular dystrophy. Research is conducted at every level, from fundamental biology to clinical intervention.

   This is not an inclusive list of all research topics covered by the Division of Musculoskeletal Diseases. To learn more, please visit the Division page at http://www.niams.nih.gov/Funding/Funding_Opportunities/Supported_Scientific_Areas/Musculoskeletal_Diseases/default.asp.

Special Emphasis Areas of Interest to Small Businesses:

NIAMS supports all Research and Development activities within its mission, Particular areas of programmatic interest relative to small business initiatives include, but are not limited to:

a. Innovation research on rare musculoskeletal, rheumatic and skin diseases

b. Multiplex assay development for arthritis and musculoskeletal and skin diseases

c. Lab to marketplace: translation of scientific discoveries in NIAMS mission areas from labs into products on the market

d. Test and/or validation of novel, state-of-the-art candidate biomarker platforms for predicting the onset and progression of inflammatory diseases of interest to the NIAMS and for determining the pharmacodynamics, safety and/or efficacy of therapeutic agents targeting those diseases.

For general SBIR/STTR program information, contact:

Dr. Xibin Wang, NIAMS SBIR/STTR Coordinator
301-451-3884, Fax: 301-480-1284
Email: wangx1@mail.nih.gov

For administrative and business management questions, contact:

Ms. Sheila Simmons
301-594-9812, Fax: 301-480-5450
Email: simmonss@mail.nih.gov

Mr. Erik (Timothy) Edgerton
301-594-3968, Fax: 301-480-5450
Email: edgertont@mail.nih.gov

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is to improve health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and medical care. This is achieved through: research and development of new biomedical imaging and bioengineering techniques and devices to fundamentally improve the detection, treatment, and prevention of disease; enhancing existing imaging and bioengineering modalities; supporting related research in the physical and mathematical sciences; encouraging research and development in multidisciplinary areas; supporting studies to assess the effectiveness and outcomes of new biologics, materials, processes, devices, and procedures; developing technologies for early disease detection and assessment of health status; and developing advanced imaging and engineering techniques for conducting biomedical research at multiple scales. More specifically, the mission of the NIBIB includes the following research areas:

A. ***Biomaterials.*** Development of new or novel biomaterials that can be used for a broad spectrum of biomedical applications such as implantable devices; drug and gene delivery; tissue engineering; imaging agents; and biosensors and actuators. Research that is supported includes the design, synthesis, characterization, processing and manufacturing of these materials as well as the design and development of devices constructed of these materials and their clinical performance.

B. ***Biomechanics and Rehabilitation Engineering.*** Research on biomechanics which can be applied to a broad range of applications including implants, prosthetics, clinical gait and posture biomechanics, traumatic injury, repair processes, rehabilitation, sports and exercise, as well as technology development in other NIBIB interest areas applied towards biomechanics. Rehabilitation engineering research that is supported includes theoretical models and algorithms for understanding neural, motor, and robotic control strategies; quantitative analysis algorithms for predicting therapeutic outcomes; and early stage development of neuroprosthesis technology, virtual rehabilitation, and robotics rehabilitation.

C. ***Biomedical Informatics.*** Development of new technologies to collect, store, retrieve, and integrate quantitative data; large-scale data-driven knowledge base and database methods that support data mining, statistical analysis, systems biology and modeling efforts; and improvement of computer science methods to protect confidentiality of patient data.

D. ***Drug and Gene Delivery Systems and Devices.*** Development of new and improved technologies for the controlled and targeted release of therapeutic agents. Areas of emphasis include: the development of new delivery vehicles such as nanoparticles and micellar systems; energy-assisted

delivery using ultrasound, electroporation, etc.; and the integration of biosensing with controlled dosage delivery using BioMEMS and other emerging technologies.

E. ***Image-Guided Interventions.*** Research on use of images for guidance, navigation and orientation in minimally invasive procedures to reach specified targets. Examples include image-guided interventions for minimally invasive therapies such as surgery and radiation treatment, for biopsies, and for the delivery of drugs, genes and therapeutic devices.

F. ***Image Processing, Visual Perception, and Display.*** Study, invention, and implementation of structures and algorithms to improve communication, understanding, and management of information related to biomedical images. Research that is supported includes software and hardware for image reconstruction, analysis, display and perception, visualization, and computer-aided interpretation.

G. ***Imaging Agents and Molecular Probes.*** Development and application of novel imaging agents and probes for clinical or pre-clinical applications. Examples of supported research include the development and application of quantum dots, nanoparticles, nanoshells, microbubbles, and radio-labelled contrast materials, and smart imaging agents that are bio-activatible or activated by other chemical, physical, or biological means.

H. ***Magnetic, Biomagnetic and Bioelectric Devices.*** Development of magnetic, biomagnetic and bioelectric devices, e.g., EEG, MEG, etc. Examples include (but are not restricted to) novel detectors, increased sensitivity and spatial resolution, improved reconstruction algorithms, multiplexing with other imaging techniques, etc.

I. ***Magnetic Resonance Imaging and Spectroscopy.*** Development of MR imaging and MR spectroscopic imaging, for both animal and human research, and potential clinical applications. Examples include (but are not restricted to) fast imaging, high field imaging, design of novel RF and gradient coils, novel pulse sequences, design of novel contrast mechanisms, imaging informatics, *in vivo* EPR imaging, molecular imaging, etc. The emphasis should be on technological development rather than detailed applications to specific diseases or organs.

J. ***Mathematical Modeling, Simulation and Analysis.*** Development of mathematical models and computational algorithms with potential clinical or biomedical applications, including multi-scale modeling, modeling at or above the cellular level, and modeling at subcellular level, including those developed to support technology development in other program areas related to the NIBIB mission. Research that is funded includes studies that focus on the development of algorithms, mathematical models, simulations and analysis of complex biological, physiological, and biomechanical systems and use genomics and proteomics.

K. ***Medical Devices and Implant Science.*** Design, development, evaluation and validation of medical devices and implants. This includes exploratory research on next generation concepts for diagnostic and therapeutic devices; development of tools for assessing host-implant interactions; studies to prevent adverse events; development of predictive models and methods to assess the useful life of devices; explant analysis; improved *in vitro* and animal models for device testing and validation.

L. ***Micro- and Nano-Systems, Platform Technologies.*** Development of BioMEMS, microfluidics and nanoscale technologies, including micro-total analysis systems, arrays, and biochips, for detection and quantitation of clinically relevant analytes in complex matrices. Application areas include biomedical research, clinical laboratory diagnostics, biodefense, high-throughput screening, drug delivery, tissue engineering, and implantable devices, among others.

M. ***Nanotechnology.*** Research and development of new enabling technologies for the fabrication and use of nanoscale components and systems in diagnostic and therapeutic applications. Examples include: development of new nanoscale patterning and manipulation systems; new approaches to the sensing and quantification of biologically important molecules using nanoscale specific properties; studies relating to the safety and commercialization of nanotechnology-enabled biomedical products.

N. ***Nuclear Medicine.*** Research and development of technologies that create images out of the gamma-ray or positron (and resulting photon) emissions from radioactive agents that are injected, inhaled, or ingested into the body and then concentrate in specific biological compartments. Two particularly active areas are the wedding of positron emission tomography (PET) and single photon emission computed tomography (SPECT) to CT and/or to MRI, and the design of higher resolution, lower cost PET and SPECT devices for the study of molecular probes in small animals. Other topics of interest include the development of better radiopharmaceuticals, crystal scintillators, and collimators, and novel approaches to dual-isotope imaging and to dosimetry.

O. ***Optical Imaging and Spectroscopy.*** Development and application of optical imaging, microscopy, and spectroscopy techniques; and development and application of optical imaging contrasts. Examples of research areas include fluorescence imaging, bioluminescence imaging, OCT, SHG, IR imaging, diffuse optical tomography, optical microscopy and spectroscopy, confocal microscopy, multiphoton microscopy, flow cytometry, development of innovative light sources and fiber optic imaging devices.

P. ***Sensors.*** Development of sensor technologies for the detection and quantitation of clinically relevant analytes in complex matrices. Application areas include (among others) biomedical research, clinical laboratory diagnostics, and biodefense, covering *in vitro* diagnostics, noninvasive monitoring, and implantable devices. Technologies encompassed include novel signal transduction approaches, materials for molecular recognition, biocompatibility, signal processing, fabrication technologies, actuators, and power sources.

Q. ***Structural Biology.*** Development of structural biology techniques, including (but not restricted to) solid state NMR, EPR, synchrotron radiation, etc. The emphasis is on technological development, rather than applications to specific structural biology problems.

R. ***Surgical Tools and Techniques.*** Research and development of new medical technologies to improve the outcomes of surgical interventions. Examples of relevant technologies include: minimally invasive surgeries, energy-based interventions such as RF ablation, robotically assisted surgical systems, integration of imaging and interventional modalities, image guided interventions and telehealth.

S. ***Telehealth.*** Development of software and hardware for telehealth studies that have broad applications as well as early stage development of telehealth technologies that may have specific focus areas. Research that is supported includes methods to address usability and implementation issues in remote settings, and methods to develop technology for standardizing and incorporating state of the art security protocols for verifying user identities and preserving patient confidentiality across remote access.

T. ***Tissue Engineering and Regenerative Medicine.*** Development of enabling technologies including real-time, non-invasive tools for assessing the function of engineered tissues; real-time assays that monitor the interaction of cells and their environment at the molecular and organelle level; predictive computational models for engineering function 3D tissues; high-throughput assays and instruments to reduce the cost, time, and complexity of tissue engineering; novel bioreactor techniques for expanding stem cells and growing tissues and organs on a large scale; and strategies for preserving, sterilizing, packaging, and transporting living-tissue products. The program also supports applications of rational engineering design principles to functional engineered tissues; the development of novel biomaterials for use as tissue scaffolds that mimic the extracellular matrix and support multiple cell types in defined spatial orientation; and engineering approaches to study how biomaterials interact with cells and guide cell growth, differentiation, and migration.

U. ***Ultrasound.*** Improvement of technologies for diagnostic, interventional and therapeutic uses of ultrasound. The diagnostic ultrasound program includes, but is not limited to the design, development and construction of transducers, transducer arrays, and transducer materials, innovative image acquisition and display methods, innovative signal processing methods and devices, and optoacoustic and thermoacoustic technology. It also includes the development of

image-enhancement devices and methods, such as contrast agents, image and data presentation and mapping methods, such as functional imaging and image fusion. The interventional ultrasound program includes the use of ultrasound for therapeutic use, or as an adjunct for enhancement of non-ultrasound therapy applications. Examples include, but are not limited to, high-intensity focused ultrasound (HIFU) as a non-invasive or minimally invasive interventional surgical or therapy tool, and as an adjunct interventional tool. It also includes the use of ultrasound contrast agents for therapy and for targeted drug delivery, and the use of ultrasound for image-guided surgery, biopsy, and other interventions.

V. ***X-ray, Electron, and Ion Beam.*** Enhancement of computed tomography (CT), computed radiography (CR), digital radiography (DR), digital fluoroscopy (DF), and related modalities. Research areas of support include the development of: flat panel detector arrays and other detector systems; flat-panel CT; CT reconstruction algorithms for the cone-beam geometry of multi-slice CT; approaches to radiation dose reduction, especially with CT; and novel x-ray applications, such as those utilizing scattered radiation, tissue-induced x-ray phase shifts, etc.

For additional information on research topics, contact:

Mr. Todd Merchak
National Institute of Biomedical Imaging and Bioengineering
301-496-8592, Fax: 301-480-1614
Email: merchakt@mail.nih.gov

For administrative and business management questions, contact:

Mr. James Huff
National Institute of Biomedical Imaging and Bioengineering
301-451-4786, Fax: 301-451-5735
Email: huffj@mail.nih.gov

NATIONAL CANCER INSTITUTE (NCI)

The National Cancer Institute (NCI) is committed to dramatically lessening the impact of cancer. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs are NCI's engines of innovation for developing and commercializing novel technologies to better prevent, diagnose, and treat cancer while enhancing cancer research and control. NCI's SBIR and STTR Programs offer funding for therapeutic agents and devices; *in vitro* and *in vivo* diagnostics, including companion diagnostics and imaging agents; agents and technologies for cancer prevention; tools for research in cancer biology, cancer control, and epidemiology; digital health, including health information technology and bioinformatics; and many more areas of interest to the NCI.

NCI's SBIR and STTR programs focus on research, development, and delivery of cancer technologies by funding small business concerns to conduct innovative research and development. The NCI SBIR Development Center is committed to helping small business concerns advance promising technologies towards the marketplace through funding as well as initiatives designed to facilitate external investments and commercialization. NCI is interested in following the progress of its funded small business concerns and the products they develop. Funding priority will be given to those small business concerns that show not only the ability to develop products but also growth towards independence from the SBIR/STTR programs.

The major NCI SBIR/STTR portfolio areas are listed below as a guide to general technology areas funded through the program. Applications proposing innovative cancer-related technologies, with strong commercial potential, that fall outside these topic areas are also invited through this Omnibus solicitation.

Major NCI SBIR/STTR Portfolio Areas:

- Therapeutics (e.g. Small Molecules, Biologics, Radiomodulators, and Cell-based Therapies)
- *In Vitro* and *In Vivo* Diagnostics (e.g. Companion Diagnostics and Prognostic Technologies)
- Imaging Technologies (e.g. Agents, Devices, and Image-Guided Interventions)
- Devices for Cancer Therapy (e.g. Interventional Devices, Surgical, Radiation and Ablative Therapies)
- Tools for Cancer Biology Research
- Technologies and Agents for Cancer Prevention
- Technologies for Cancer Control (e.g. Behavioral Health Interventions, Tools for Genetic, Epidemiologic, Behavioral, Social, and/or Surveillance Cancer Research)
- Digital Health (e.g. Mobile Health, Health Information Technology, and Bioinformatics)

NCI particularly encourages applications in the following current research topics of interest:

- Development of Low Cost Technologies for Global Health
- Development of Companion Diagnostics
- Vaccine Development for Cancer Prevention
- Novel Technologies to Address “Undruggable” Drug Targets
- New Technologies to Assess Tissue-Based Markers of Tumor Death and Mitochondrial Stress in Response to Therapy

NCI accepts and encourages SBIR/STTR applications to support clinical trials.

For up-to-date information on high priority technology areas, and to learn about programmatic initiatives and upcoming events, visit the NCI SBIR Development Center homepage: http://sbir.cancer.gov/.

In addition, please see the contact list at the end of the NCI section to identify the Program Director within the NCI SBIR Development Center who specializes in your technology area.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NCI may decide not to fund an application or may decrease the length of an award and/or the budget recommended by a review committee. Generally, NCI will not fund Phase I applications greater than $225,000 total costs or project periods greater than 2 years; nor Phase II applications greater than $1,500,000 total costs or project periods greater than 3 years. For certain topical areas (http://bit.ly/NCIwaiver), the Small Business Administration has approved an NIH SBIR/STTR Topic Waiver list for which the NCI generally will not fund Phase I applications greater than $300,000 total costs or project periods greater than 2 years; nor Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years. Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB SBIR Competing Renewal Awards

The NCI does not accept applications for Phase IIB SBIR competing renewal award through this Omnibus solicitation. However, the NCI offers Phase IIB opportunities in the form of the NCI SBIR Bridge Award, which is announced via a separate funding solicitation. The SBIR Bridge Award is designed to support the next stage of development for previously funded NIH-wide SBIR Phase II projects in the areas of cancer

therapeutics, imaging technologies, interventional devices, diagnostics and prognostics. The purpose of this award is to address the funding gap known as the "Valley of Death" between the end of the SBIR Phase II award and the subsequent round of financing needed to advance a product or service toward commercialization. To achieve this goal, the Bridge Award funding opportunity is specifically designed to incentivize partnerships between NIH's SBIR Phase II awardees and third-party investors and/or strategic partners. Competitive preference and funding priority will be given to applicants that demonstrate the ability to secure substantial independent third-party investor funds (i.e., third-party funds that equal or exceed the requested NCI funds).

Budgets up to $1 million in total costs per year and project periods up to three years (a total of $3 million over three years) may be requested from the NCI. Development efforts may include preclinical R&D needed for regulatory filings (e.g., IND or IDE) and/or clinical trials. NCI intends to commit up to $10M for up to 10 new awards in FY2015.

To ensure that you will be notified upon the release of the NCI SBIR Phase IIB Bridge Award solicitation, please sign up for the NCI SBIR mailing list. If you have any questions regarding the Bridge Award, please contact your Phase II program director.

For additional information about the NCI SBIR/STTR programs, please contact the NCI SBIR Development Center:

Small Business Innovation Research (SBIR) Development Center
National Cancer Institute
9609 Medical Center Drive
Rockville, MD 20850
Website: http://sbir.cancer.gov
Email: NCIsbir@mail.nih.gov
Phone: 240-276-5300

For additional information on research topics, please contact a Program Officer with the relevant area of expertise:

Michael Weingarten, MA
Director, NCI SBIR Development Center
Email: weingartenm@mail.nih.gov

Gregory Evans, PhD
Program Director and Team Leader
Email: evansgl@mail.nih.gov

Areas of expertise: Therapeutics (Immunotherapy, Gene Therapy), Cancer Imaging, Cancer Control, Tools for Cancer Biology Research, and Digital Health

Andrew Kurtz, PhD
Program Director and Team Leader
Email: kurtza@mail.nih.gov

Areas of expertise: Therapeutics (Small Molecules, Biologics, Nanotherapeutics), and Molecular Diagnostics

Patricia Weber, DrPH
Program Director
Email: weberpa@mail.nih.gov

Areas of expertise: Digital Health and Therapeutics (Small Molecules, Biologics, Immunotherapy)

Xing-Jian Lou, PhD
Program Director
Email: loux@mail.nih.gov

Areas of expertise: *In Vitro* Diagnostics and Therapeutics (Gene Therapy)

Deepa Narayanan, MS, CCDM
Program Director
Email: narayanand@mail.nih.gov

Areas of expertise: Radiation Therapy, Cancer Imaging, Medical Devices, and Clinical Trials

Amir Rahbar, PhD, MBA
Program Director
Email: amir.rahbar@nih.gov

Areas of expertise: *In Vitro* Diagnostics, Proteomics, and Therapeutics (Biologics)

Todd Haim, PhD
Program Director
Email: haimte@mail.nih.gov

Areas of expertise: Therapeutics (Small Molecules, Biologics, Immunotherapy) and Cancer Prevention

Ming Zhao, PhD
Program Director
Email: zhaoming3@mail.nih.gov

Areas of expertise: *In Vitro* Diagnostics, Cancer Stem Cells, Molecular Imaging, Bioinformatics, Therapeutics (Small Molecules, Biologics, Immunotherapy), and Cancer Control (Community-Based Participatory Research)

Jennifer Shieh, PhD
Program Director
Email: jennifer.shieh@nih.gov

Areas of expertise: Digital Health, Bioinformatics, and Research Tools

For administrative and grants management questions, please contact:

Jacquelyn Boudjeda
Grants Management Specialist
Office of Grants Administration
National Cancer Institute
9609 Medical Center Drive
West Tower, 2W514
Rockville MD 20850
240-276-6312
Fax: (240) 276-7913
Email: boudjedaj@mail.nih.gov

For NCI-related SBIR Information, visit: http://sbir.cancer.gov.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

The mission of the NICHD is to ensure that every person is born healthy and wanted, that women suffer no harmful effects from reproductive processes, and that all children have the chance to achieve their full potential for healthy and productive lives, free from disease or disability, and to ensure the health, productivity, independence, and well-being of all people through optimal rehabilitation.

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

Budget Guidelines

For NICHD award topic areas included in PHS 2014-2 Omnibus Solicitation, the NICHD will accept SBIR/STTR applications up to $225K total costs for Phase I and $1.5M for Phase II. Requests for costs above the SBIR/STTR budgetary guidelines of $150K for Phase I and $1M for Phase II must be very well justified.

The NICHD received a budgetary guideline waiver from the Small Business Administration for applications relating to the limited list of scientific topics (Appendix A). For these the NICHD will accept applications up to $300K total costs for Phase I and $2M for Phase II. Requests for costs above the guidelines of $150K for Phase I and $1M for Phase II must be very well justified.

Applicants are strongly encouraged to contact the listed NICHD Branch Contact Program Officer for scientific-related questions about a project's eligibility for a budgetary waiver. For general budgetary questions applicants are encouraged to contact the Institute's SBIR/STTR Grants Management Coordinator.

Phase IIB Competing Renewal Awards

NICHD will accept Phase IIB SBIR 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, pediatric devices, 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 NICHD SBIR Phase I or Phase II support and who are currently Phase II awardees are eligible. Budgets for Phase IIB renewals should not exceed 3 million dollars total costs for three years. Depending on the research proposed the amounts may vary each year for the time requested.

You are strongly encouraged to contact Dr. Louis Quatrano or the Program Contact listed at the end of each topic area before beginning the process of putting a Phase IIB 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-12-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 Phase IIB 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.

NICHD Topic Areas

CHILD DEVELOPMENT AND BEHAVIOR BRANCH (CDBB)

The CDBB encourages developmentally-sensitive evidence-based small business initiatives that develop technology and products addressing the psychological, social and emotional, psychobiological, language, numerical, literacy, cognitive and intellectual development and health of persons from infancy to maturity. Products that exploit electronic and mobile technologies in order to encourage healthy development and/or our understanding of the influences of context and/or behavior on development are especially encouraged.

Foci of specific interest include, but are not limited to (please also see the CDBB description):

- Intervention programs for social-emotional health and skill development in children, intervention programs for the prevention of child abuse and neglect in at-risk populations, web-based training programs to enhance parenting skills, novel technologies related to the assessment of emotion, or new tools or methods to enhance the study of human-animal interactions.
- Tools for functional assessment of brain processes in young children, new approaches for quantification of behavior with animal models and tools for facilitating memory and learning in children and adolescents.
- Innovative technologies, devices, and programs that address behavioral and developmental aspects of health risk behaviors and health promotion from infancy to young adulthood. It encourages research that will promote health and healthy behaviors such as sleep, eating habits, physical activity, prosocial behaviors, academic achievement, literacy, medical care, adherence to medication and to medical advice, and/or reduce pain, obesity, sedentary behavior, risky behaviors (i.e. sex, substance abuse, unsafe driving) from infancy to young adulthood.
- Tools to address reading, writing, and related learning disabilities such as assistive technologies, interactive technologies for use by children, adolescent or adult struggling learners as well as technologies for instructors, parents and/or caregivers for use within or outside of the classroom context, as appropriate.
- Assistive technologies or interactive technologies for use by at-risk or struggling primary and/or second language learners (of any age cohort from birth through young adulthood) in any context Development and testing of new technology-based interventions and learning tools whose primary focus is the promotion of early learning and the development of school readiness skills and abilities, including those designed to target specific subpopulations of children and their families (e.g., English Language Learners (ELLs)).
- Innovative technology-based methods and assessments for measuring early learning and school readiness skills and abilities and measures of home, child care and preschool environments and practices that are related to child learning and development.
- Innovative technologies that address behavioral and developmental aspects of mathematical thinking and problem solving; scientific reasoning, learning, and discovery.
- Assistive or instructional technologies for use by at-risk or struggling learners of any age cohort from birth through young adulthood in any context (e.g., home, school, work) where improved learning, understanding and/or reasoning is needed.

Dr. Kathy Mann Koepke
301-435-6855, Fax: 301-451-565
Email: KMK@nih.gov

CONTRACEPTIVE DISCOVERY AND DEVELOPMENT BRANCH

Emphasis is on developing new and improved methods of fertility regulation as well as research on the benefits and risks of contraceptive drugs, devices and surgical procedures. Areas of interest include, but are not limited to:

- Development of new and improved methods of fertility regulation, for men and women, that are safe, effective, inexpensive, reversible and acceptable.
- Validation and characterization of targets whose modulation may be contraceptive.
- Synthesis and testing of novel chemical compounds that are potential contraceptives.
- Studies relating contraception to STDs such as HIV, including but not limited to development of new contraceptive products combined with products with microbicidal activity against STDs such as HIV.
- Studies to clarify the mechanism of interaction between contraception and other disease processes or conditions.
- Small molecule lead discovery through screening targeted and natural product compound libraries on validated male and female contraceptive targets.
- Screening non-traditional sources of natural products on validated male and female contraceptive targets.
- Medicinal chemistry component in support of drug design and synthesis on validated male and female contraceptive targets.
- Integrated computational/modeling, fragment library screening, structure biology, medicinal chemistry and biological screening infrastructures for structure based drug discovery (SBDD).
- Discovery and validation of male and female specific targets involved in control of fertility through research on the processes of spermatogenesis, follicular development, ovulation or fertilization.

Dr. Steven Kaufman
301-435-6989, Fax: 301-480-1972
Email: Kaufmans@exchange.nih.gov

DEVELOPMENTAL BIOLOGY AND STRUCTURAL VARIATION BRANCH

Biomedical research on the cellular, molecular, and genetic aspects of normal and aberrant embryonic and fetal development including early embryogenesis, organogenesis, limb regeneration, development of the nervous system, and causative factors in teratogenesis, as well as related topics on regeneration [e.g. limb, CNS, etc.] and regenerative medicine. Areas of interest include but are not limited to:

- development and application of new animal model systems
- in vivo techniques for optical imaging and quantitative measurement of physical properties of cells/tissues
- innovative technologies for imaging developmental processes and gene expression
- innovative and high throughput genomic and proteomic techniques
- technologies to facilitate and advance systems biology approaches to the study of embryonic development and structural birth defects, or regeneration
- in vivo techniques for optical imaging and quantitative measurement of physical properties of cells/tissues
- innovative technologies to facilitate and advance high throughput plating of zebrafish embryos, larva, and adults to facilitate chemical screening
- software development to facilitate the collection and analyses of data generated through the use of high throughput screening platforms using zebrafish embryos, larva, and adults
- technologies/methodologies to generate and software to mine data related to wound healing and regenerative responses across animal species
- technologies for iPS cell-based regenerative medicine

- development of novel ligands, promoters and other probes that can facilitate regenerative mechanisms

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

FERTILITY AND INFERTILITY BRANCH

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:

- Development of reagents to facilitate study of reproductive and developmental processes.
- Development of improved methods of growing and differentiating stem cell lines *in vitro*, including feeder cell-free approaches.
- Development of novel assays, kits, and devices to monitor fertility and treat infertility and gynecological disorders.
- Use of genomics and proteomics to develop novel diagnostics and treatments for reproductive diseases and disorders.
- Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
- Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.
- Development of improved and novel technologies for the preservation of human gametes.
- Development of improved technologies for preimplantation genetic diagnosis.
- Development of improved technologies for the reprogramming of cells, including embryonic stem cells or adult cells, into eggs and sperm.

Dr. Stuart Moss
301-435-6979, Fax: 301-496-0962
Email: mossstua@mail.nih.gov

GYNECOLOGIC HEALTH AND DISEASE BRANCH

Emphasis is on biomedical research on gynecologic health issues in women and adolescent girls. Areas of research include pelvic floor disorders, the menstrual cycle, uterine fibroids, endometriosis, the perimenopause/menopause, chronic pelvic pain, vulvodynia and dysmenorrhea. Areas of interest include, but are not limited to:

- Developing new and improved diagnostic approaches and treatments for female pelvic floor disorders, including drugs, graft materials, and devices used for non-surgical and surgical treatment of pelvic organ prolapse, urinary incontinence, and other female pelvic floor disorders.
- Development of new diagnostic approaches and treatments for uterine fibroids, endometriosis, abnormalities of the menstrual cycle and symptoms associated with the perimenopause/menopausal transition.
- Research on mechanisms, diagnosis and treatment of gynecologic pain disorders including chronic pelvic pain, vulvodynia and dysmenorrhea.

Dr. Estella Parrott
Phone: 301-435-6971, Fax: 301-480-1972
Email: parrotte@mail.nih.gov

INTELLECTUAL AND DEVELOPMENTAL DISABILITIES BRANCH

The IDD Branch sponsors research aimed at preventing, diagnosing, and ameliorating intellectual and developmental disabilities (IDD). Emphasis is on studies related IDD, including common and rare neuromuscular and neurodevelopmental disorders, such as Down, Fragile X, and Rett syndromes, mitochondrial conditions, inborn errors of metabolism, autism spectrum disorders, and others. Areas of interest include, but are not limited to:

- Studies designed to understand the etiology and pathophysiology of abnormal nervous system development
- Studies designed to delineate genetic, genomic, and epigenetic bases of IDD
- Studies designed to examine the screening, diagnosis, treatment, and management of IDD and other conditions identified by newborn screening or other screening methods
- Studies that promote multidisciplinary and translational research in IDD through programs that integrate basic and applied research, training, and service activities
- Studies that advance efforts toward the prevention and diagnosis of IDD as well as early intervention and treatment for these conditions.

Dr. Tiina K. Urv
301-402-7015, Fax: 301-496-3791
Email: urvtiin@mail.nih.gov

MATERNAL AND PEDIATRIC INFECTIOUS DISEASE BRANCH

Domestic and international research on human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) and related infections (such as tuberculosis, hepatitis and malaria) in women of child bearing age, pregnant women, mothers, fetuses, infants, children and adolescents. Specific areas of interest include but are not limited to epidemiology, clinical manifestations, pathogenesis, transmission, treatment and prevention (including vaccines and other biomedical modalities) of HIV infection and other infectious diseases in children, adolescents and pregnant women, including prevention of mother to child transmission of HIV and other congenital infections, and HIV-related and other infectious-disease related complications in these populations. Additional areas of interest include:

- New technologies relevant to resource-limited countries for:
    - diagnosis of HIV infection and other infectious diseases in infants;
    - diagnosis and treatment of HIV-related complications of HIV (e.g., diagnosis of tuberculosis in children);
    - simple and less technical point of care assays to monitor CD4 cell percentage/count, HIV viral load, or other surrogate markers of HIV disease progression in children.

- Drug formulations for antiretroviral drugs and/or drugs used to treat complications of HIV infection such as tuberculosis, hepatitis, and malaria relevant to children (preferably not liquid preparations), particularly in resource-limited countries and including fixed dose drug formulations and innovative methodologies for development of solid formulations capable of being administered to young children (e.g., sustained release beads, etc).
- Innovative long-lasting drug formulations for antiretroviral and other anti-infective drugs that would allow less frequent drug administration (e.g., once daily, weekly or monthly).
- Simple, standardized tools to evaluate neurodevelopmental outcome in children in resource-limited settings.
- Biomedical modalities, including vaccines, to prevent acquisition of HIV and other infectious diseases in children, adolescents and women.
- Topical microbicide agents to prevent sexual acquisition of HIV and other STDs in women or in adolescents.

- New, non-invasive technologies to evaluate complications of antiretroviral drugs in HIV-infected infants, children, adolescents (e.g., mitochondrial toxicity) and pregnant women, their fetuses and children.

Dr. Lynne Mofenson
301-435-6870; Fax: 301-496-8678Email: LM65D@nih.gov

OBSTETRIC AND PEDIATRIC PHARMACOLOGY AND THERAPEUTICS BRANCH

The OPP Branch promotes research to improve the safety and efficacy of pharmaceuticals and to ensure centralization and coordination of research, clinical trials, and drug development activities for obstetric and pediatric populations. This includes developing and supporting a comprehensive national effort to increase the knowledge base for understanding how to appropriately treat disease during pregnancy, infancy, and childhood using pharmaceuticals that are appropriately tested within their target populations.

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 pharmacokinetic/pharmacodynamics modeling which improve therapy during pregnancy, among premature infants, children and adolescents;
- research on devices to monitor the state of various organ systems during therapy in pregnancy or infancy;
- development of non-invasive devices for evaluating adherence to chronic therapy in life-threatening conditions (e.g. HIV, diabetes, asthma, liver and kidney transplantation);
- development of novel approaches for oral mucosal, transdermal, nasal, ocular and pulmonary drug delivery systems and device technologies.
- Use of a materials science approach to overcome solubility limitations of pediatric drugs, increase bioavailability, decrease excipient exposure, and provide effective taste masking.
- Development of nanosized formulations to optimize efficacy and minimize toxicity of pediatric drugs
- identification of targets for pregnancy associated/induced diseases that can lead to the development of new targeted therapeutics for diseases like pre-eclampsia, gestational diabetes, preterm labor.

Dr Anne Zajicek
301 435-6865, Fax: 301-480-2897
E-mail: zajiceka@mail.nih.gov

PEDIATRIC GROWTH AND NUTRITION BRANCH

The PGN branch supports research designed to lay the groundwork for future health so that children can achieve their full potential for growth and development. The burden of metabolic syndrome, obesity, cardiovascular disease, diabetes, and osteoporosis continue to increase in this country and abroad. These chronic conditions have their roots in infancy or childhood and are difficult or impossible to reverse in adulthood. The PGN encourages research that focuses on detecting the earliest aberrations in molecular and biochemical pathways that lead to disease later in life. Areas of interest include, but are not limited to:

- Physical growth, body composition, bone health, nutrition, and obesity.
- Determinants of normal bone mineral accretion and peak bone mass. Interactions of muscle and bone during infancy and childhood.
- Neuroendocrinology of puberty, linear growth, obesity, and malnutrition.
- Prevention of chronic diseases such as diabetes, osteoporosis and metabolic syndrome.

- Genetic and molecular mechanisms of obesity, psychosocial risks of obesity, and therapeutic interventions for obesity.
- Mechanisms of hormone action during linear growth, pubertal maturation, and other aspects of development.
- Novel approaches to Type-1 Diabetes management and treatment, especially related to the development of the artificial pancreas.
- Technological innovations/inventions to diagnose and monitor diabetes.
- Nutritional requirements during pregnancy
- Aspects of nutrients related to growth and disease prevention during infancy and childhood.
- Training of the next generation of pediatrician scientists.

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

PEDIATRIC TRAUMA AND CRITICAL ILLNESS BRANCH

The PTCI branch develops and supports research and research training in pediatric trauma and critical illness; investigates the continuum of psychosocial, behavioral and physiological influences that impact child health outcomes in trauma, injury and acute care; investigates the short and long term impacts of acute traumatic experiences such as natural and man-made disasters, all forms of child maltreatment, violence and violence exposure; develops research linking pediatric emergency and critical care medicine and science to the epidemiology, prevention, and treatment of childhood physical disabilities; and supports research on prevention, treatment, management, and outcomes of physical and psychological trauma and the surgical, medical, psychosocial and systems interventions needed to improve outcomes for critically ill and injured children across the developmental trajectory. Applications of interest include, but are not limited to:

- Research and development on pediatric-specific technologies and equipment used by emergency and trauma care personnel.
- Development of tools and technologies for efficient screening and determination of the nature of injury, bruising related to forms of child maltreatment.
- Research and development of devices and innovative therapeutic technologies for management of physical disabilities and related problems stemming from and acute injuries.
- Development of preventive intervention tools, materials, and technologies designed to improve clinical practice, parenting and social system support for injured children and children exposed to violence.

Dr. Valerie Maholmes
301-496-1514, Fax: 301-480-0230
Email: Maholmes@mail.nih.gov

POPULATION DYNAMICS BRANCH

The PD Branch supports research and research training in demography, reproductive health, and population health. In **demography**, the Branch supports research on the scientific study of human populations, including fertility, mortality and morbidity, migration, population distribution, nuptiality, family demography, population growth and decline, and the causes and consequences of demographic change. In **reproductive health**, the Branch supports behavioral and social science research on sexually transmitted diseases, HIV/AIDS, family planning, and infertility. In **population health**, the Branch supports data collection and research on human health, productivity, behavior, and development at the population level, using such methods as inferential statistics, natural experiments, policy experiments, statistical modeling, and gene/environment interaction studies.

Applications are encouraged, but are not limited to these areas:

- Technological innovations or inventions to improve collection of biomarker data in large population-representative surveys.
- Hardware or software to improve collection of accurate cause of death information or health diagnosis in large population-representative surveys or in administrative data sets.
- Methods for integrating geographical information systems (GIS), spatial network analysis, and/or simulation methods for demographic research.
- Methods for improving collection, documentation, archiving, and dissemination of population representative data sets, including especially data sets that are complex, multilevel or multimodal.
- Methods for protecting and assuring confidentiality for human subjects when collecting, archiving, or disseminating population-representative data sets, especially data sets that are longitudinal or that include both spatial and individual-level data.
- Methods for reducing cost of collecting and disseminating large-population-representative data sets.
- Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, at risk youth, and other health-related topics.
- Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.
- 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. Susan Newcomer
301-435-6981, Fax: 301-496-0962
Email: newcomes@mail.nih.gov

PREGNANCY AND PERINATOLOGY BRANCH

The PP branch supports research in the following areas: 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. The following topic areas are of high priority:

Neonatal:

- Non-invasive methods for assessing cardiovascular and pulmonary functions, including cardiac output, systemic blood pressure, airway resistance, pulmonary compliance, vital capacity and various lung volumes.
- Metabolic profile assessment using non-invasive or minimally invasive approaches. Particular area of expertise include measurement of glucose and lactate/pyruvate; assessing ketone body measurements; free indirect bilirubin (unconjugated, free indirect); major chemicals (Na^+ Ca^+ Cl^+ K^+ etc.) in the blood.
- Improved point of care methods to measure plasma glucose concentrations quickly and accurately.

- Devices, instruments, and tools to minimize bacterial colonization, reduce proclivity for thrombous formation; reduce health-care associated infection risks.
- Rapid methods for diagnosis of bacterial infections and inflammation.
- Non-invasive measures to assess brain energy utilization, especially glucose, oxygen, lactate, ketones, and other energy substrates.
- Innovative ideas to reduce stress for the staff, parents and infants in the NICU.

Perinatal :

- Non-invasive (or minimally invasive) methods to assess fetal well-being
- Non-invasive (or minimally invasive) methods to assess placental anatomy, physiology and function.
- Methods to predict spontaneous preterm birth.
- Methods to predict preeclampsia.

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

NATIONAL CENTER FOR 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 but are not limited to:

- Systems Science - Develop methodologies/models for data to address the health trajectories from pathophysiology to participation in the rehabilitation process. Utilize methodology to understand whole body system responses to physical impairments and functional changes.
- Neuroplasticity - Develop non-invasive and surrogate measures of neuroplasticity that would be appropriate for use in a clinical setting to monitor rehabilitation treatment effectiveness.
- Rehabilitation Interventions - Develop Virtual Reality, simulations, e-health and other approaches to promote participation, understand and support healthy behaviors, reduce health disparities and enhance clinical compliance especially in children with disabilities
- Rehabilitation in the Community - Strategies to build or modify community resources that provide effective rehabilitation and health promotion services within the individual's own community.
- Novel Technology – Using nanomaterials, biomarkers, imaging, and robotics to improve rehabilitation treatment for restoration of function. Develop techniques to improve/maximize parameters for trans-cranial magnetic stimulation.

Investigators proposing budgets exceeding the guidelines are encouraged to contact program staff six weeks prior to submitting the application.

For additional information on research topics, contact:

Louis A. Quatrano, Ph.D.
Ph: 301-402-4221, Fax: 301-402-0832
Email: Quatranol@mail.nih.gov

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

For additional information on research topics, contact:

Louis A. Quatrano, Ph.D.
Eunice Kennedy Shriver National Institute of Child Health and Human Development
301-402-4221, Fax: 301-402-0832
Email: Quatranol@mail.nih.gov

For administrative and business management questions, contact:

Mr. Ted Williams
Grants Management Specialist
Eunice Kennedy Shriver National Institute of Child Health and Human Development
301-435-6996, Fax: 301-451-5510
Email: williate@mail.nih.gov

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/.

SBIR and STTR programs at NIH are primarily intended to encourage private-sector commercialization of technology and to increase small business participation in federally funded R&D.

Both the SBIR and STTR programs consist of the three phases. During Phase I, NIDA supports the projects which establish the technical merit and feasibility of proposed research / R&D efforts and determines the quality of performance of the applicant (small business concern or SBC) before providing further Federal support in Phase II. Provided that the feasibility is established, during Phase II, NIDA supports research or R&D efforts initiated in Phase I. During Phase III, SBC is to pursue commercialization with non-SBIR/STTR funds (either Federal or non-Federal). Applicants are encouraged to seek commitment(s) of funds and/or resources from an investor or partner organization for commercialization of the product(s) or service(s) resulting from the SBIR/STTR grant. Phase III funding may be from any of a number of different sources including, but not limited to: private, venture capital firms, investment companies, joint ventures, R&D limited partnerships, strategic alliances, research contracts, sales of prototypes (built as part of this and/or other project), public offering, state finance programs, non SBIR-funded R&D or production commitments from a Federal agency for use by the United States government or other industrial firms. NIDA monitors SBC efforts to pursue, with non-SBIR/STTR funds, the commercialization of the results of the research or R&D funded in Phases I and II of the SBIR/STTR Program.

NIDA funding decisions will be based on combination of factors:

- programmatic priorities (for current priorities, see NOT-DA-11-020 http://grants.nih.gov/grants/guide/notice-files/NOT-DA-11-020.html)
- potential for commercialization and public health benefit
- whether the similar projects have already been funded (for reference, search http://projectreporter.nih.gov/reporter.cfm)
- the results of Phase I and the commercial potential and scientific/technical merit of the Phase II application (for Phase II applications);
- the quality of performance of the applicant, with emphasis on prior applicant success in Phase III;

- the peer review scores and critique;
- availability of funds.

Special Features of NIDA SBIR Program

AMOUNT OF AWARD

According to recent statutory guidelines, total funding support levels (including direct costs, indirect costs, and fee) are $150,000 for Phase I awards and $1,000,000 for Phase II awards. NIDA will only consider applications to exceed these amounts if: 1) applications are in areas of programmatic priority, AND 2) there is an appropriate and strong justification from the applicant. Areas of interest are described elsewhere in this PHS (e.g. Program Descriptions and Research Topics and APPENDIX A) and in the NOT-DA-11-020. If adequate justification is provided, applicants may request up to $350,000 in total costs with the project period up to 2 years; or up to $2,500,000 in total costs with the project period up to 3 years for Phase II). Applications outside of the areas of current strategic interest will be funded at the levels of statutory guidelines ($150,000 for Phase I and $1,000,000 for Phase II, total costs). Areas of interest are described elsewhere in this PHS and in the NOT-DA-11-020. Applicants are strongly encouraged to contact NIDA program officials prior to submitting any application. For programmatic, budgetary or administrative reasons, NIDA may decrease the length of an award and/or the budget, or not fund an application.

FAST-TRACK APPLICATIONS

Important consideration for NIDA Fast-Track Mechanism:

- Convincing preliminary data
- Clear, measurable, achievable milestones
- Well-conceived Commercialization Plan
- Letters of Phase III support/interest encouraged
- Track record/previous success in commercializing product or services
- Discussion with NIH Program Staff strongly encouraged

The NIH Fast-Track mechanism expedites the decision and award of SBIR and STTR Phase II funding by incorporating a submission and review process in which both Phase I and Phase II grant applications are submitted and reviewed together. The Fast-Track application will receive a single rating for the entire proposed project (i.e., it will receive a numerical score or it will receive an “unscored” designation). To be eligible for the Fast-Track option, the Phase I Research Plan must include well-defined, quantifiable milestones that should be achieved prior to initiating Phase II work. In addition, as is required for all Phase II applications, the Phase II portion of a Fast-Track application must present a well-defined Commercialization Plan. NIDA encourages Fast-Track mechanism for scientifically meritorious applications that have expressly high potential for commercialization. Applicants considering a Fast-Track application are strongly encouraged to contact program staff BEFORE submitting an application. NIDA staff will assist the applicant in determining whether the proposed project addresses NIDA’s programmatic priorities, and whether the proposed project satisfies NIDA’s criteria for Fast Track mechanism. Potential Fast-Track applicants are encouraged and expected to discuss with the NIDA program staff the following:

- **Value of the SBIR/STTR Project** - the public/market need addressed, specifying weaknesses in the current approaches to meet this need; the commercial applications of the research and the innovation inherent in this application.
- **Expected Outcomes and Impact** - the proposed project and its key technology objectives; the product, process, or service to be developed in Phase III; the potential societal, educational, and scientific benefits of this work; the non-commercial impacts to the overall significance of the project.

- **Market, Customer, and Competition** - the market and/or market segments targeted, a brief profile of the potential customer, significant advantages SBC's innovation will bring to the market, e.g., better performance, lower cost, faster, more efficient or effective, new capability; the hurdles to overcome in order to gain market/customer acceptance of the proposed innovation; any strategic alliances, partnerships, or licensing agreements already in place to market and sell the product, FDA approval (if required), marketing and sales strategy, overview of the current competitive landscape and any potential competitors over the next several years, etc.

PHASE IIB COMPETING RENEWAL AWARDS

NIDA will accept SBIR/STTR Phase IIB Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue advancing a developing medication for the treatment of Substance Use Disorders (SUDs) to the marketplace. Such products might include (but are not limited to) small molecule drugs and biological agents such as antibodies and vaccines. The financial and time constraints of Phase I and Phase II SBIRs present significant obstacles in the advanced stage development of medications. While Phase I and Phase II SBIR support maybe sufficient for initial discovery and development efforts (e.g., compound synthesis and some *in vitro* and *in vivo* preclinical pharmacological testing), it may not be sufficient to conduct clinical trials or even fully support generation of the preclinical data package needed for an Investigational New Drug (IND) application. The purpose of Phase II Competing Renewal Award is therefore, to provide a Phase II project the possibility of another three years of support. Only a fraction of NIDA SBIR/STTR Phase II awards will likely be eligible for a Phase IIB Competing Renewal award, and applications are considered in a similar pool as new Phase II applications. One key criterion for eligibility for a Phase IIB Competing Renewal award is that the project is sufficiently close to a marketable position that a Phase 2B award could significantly advance the product to the marketplace. A second and equally important criterion is that the Phase2 award results and current market conditions are such that the project continues to be deemed to be of high impact ie, a high significance project with a similarly high likelihood of a successful outcome. Therefore, the outcome of studies conducted under the previous grant phases should be included in the justification and should provide a sound and convincing rationale for continued development of the medication. Prospective Phase IIB Competing Renewal applicants are strongly encouraged to consult with NIDA staff prior to submission in order to gauge programmatic interest in continued development. The consultation should include provision of 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

Phase IIB Competing Renewal applications may focus on development efforts for medications targeted towards attainment of abstinence and/or relapse prevention for SUD patients with stimulant (eg cocaine and methamphetamine), opiate, cannabis or nicotine dependence. Medications for emergency room management / stabilization of patients with acute toxic reactions to drugs, would also be appropriate for Phase 2b Competing Renewal applications. Agents currently recognized as presenting such concerns include stimulants such as cocaine, amphetamines and cathinones (Bathsalts), as well as synthetic drugs such as phenethylamines and the thermogenic empathogens (eg, "Ecstacy"/ "Molly").

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

- Pharmacological and toxicological studies, designed to provide data for preclinical studies section of an IND application.
- Chemistry Manufacturing & Control (CMC) studies to provide data for an IND application

- Human laboratory clinical trials (First in Man) / Escalating Dose studies 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.

For more information, contact:

Aidan Hampson, Ph.D.
Program Officer, Medications Research Grants Branch (MRGB)
Div. of Pharmacotherapies and Medical Consequences of Drug Abuse
NIH - National Institute on Drug Abuse (NIDA)
6001 Executive Boulevard
Room 4153, MSC 9551
Bethesda, MD 20892
Express mail/courier use: Rockville, MD 20852
Tel: 301-443-8039, Fax: 301-443-9649
Email: aidan.hampson@nih.gov

Research Topics of Interest to NIDA

In this Omnibus Solicitation, NIDA emphasizes its need to discover, evaluate and develop medications (both small molecules and biologics) to treat substance use disorders (SUDs). NIDA further emphasizes an importance of fostering research through NIDA SBIR/STTR Program aimed at the research and development of medications for SUD, as well as research aimed at modernizing the drug discovery and development toolkit.

High programmatic priority will be given to research that seeks to achieve these goals in the following ways:

1) Drug discovery and development-enabling activities: Development of innovative technologies, methods or tools, including but not limited to:

   - Innovative *in vitro*, in situ, or *in vivo* tools for the molecular analysis of the central nervous system, normal and/or diseased.
   - Tools to simplify drug design through the use of advanced computing (simulation) methods.
   - Development of pre-clinical models for addiction.
   - Creation of a data repository / software tools for addiction-related clinical research data.
   - Novel analytical technologies and methods that enhance the understanding of basic mechanisms of drug action and improve drug testing; technologies designed to overcome the performance limitations of current drug discovery and development tools.
   - Technologies, including molecular imaging, gene expression profiling, and genotyping and sequencing approaches designed to better inform the diagnosis and treatment of substance use disorders

2) Drug discovery and development activities: Application of emerging and existing technologies and platforms to SUD drug development. 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. Medical products with potential to minimize drug seeking, compulsive behavior, and/or addictive processes are strongly encouraged.

- Chemistry / pharmaceutical drug development
- Formulation and/or enhanced delivery of drugs
- Preclinical and/or clinical drug development
- Development of biomarkers related to treatment outcomes

Research Topics which are not aimed at development of medications for substance-use disorders or at modernizing the drug discovery and development toolkit, are accepted but are currently considered to have a low program priority.

EXAMPLES OF TOPICS OF NIDA INTEREST ARE PRESENTED BELOW:

Development of Assays for "Designer" Drugs of Abuse Based on Pharmacologic Activity Rather Than Chemical Structure. Contemporary illicit drug chemists have turned to the pharmacology literature to produce new "designer" drugs of abuse including (but not limited to) synthetic cannabinoid analogues found in “herbal incense” mixes or substituted cathinone stimulants sold as “bath salts”. This new strategy has resulted in a diverse range of potential modified structures, all of which maybe pharmacologically active but each of which varies in molecular weight and substituents. This presents a substantial complication to traditional toxicology screens conducted in Emergency Rooms and to drug testing laboratories, whose assays rely on either immuno-assays or mass-spectrometry to detect specific agents. The current Funding Opportunity Announcement therefore aims to sponsor the development of assays based on pharmacologic activity rather than chemical structure.

Such assays should be:

- Non-invasive and able to detect quantities of illicit materials or metabolites in a range of concentrations typically found biofluids of substance users within a few days of use.

- Access to the biofluid samples should be minimally invasive and provide for temporal analysis. Such sample types include blood, urine, sweat and oral fluids.

- Assays should be designed with a standard clinical or analytical laboratory in mind, i.e., to be analyzed in a high throughput format by technicians with a moderate scientific training.

- The assays can be either designed to be analyzed with standard existing equipment, or include both the assay and development of analytical hardware, provided that the ultimate system can be commercially viable in a clinical and drug testing market place.

- Assays should be designed to remain relevant as illicit substance chemists adapt to legislation by altering pharmacophoric substituents such as side chains. Examples of such assays would include (but be not limited to) scintillation proximity assays, robust cell-based assays to detect pharmacology rather than a particular chemistry, or cells expressing engineered receptors activated solely by synthetic ligands, designed to pick up a range of metabolites. Other examples might include microfluidic surface plasmon resonance devices, which can both concentrate and detect receptor or antibody-bound substances.

Aidan Hampson, Ph.D.
301-443-8039
Email: aidan.hampson@nih.gov

Discovery of New Chemical Probes. SBIR applications are encouraged which propose to discover new chemical compounds as biological probes either by synthesis or isolation from natural resources in studying the mechanisms of action of drugs of abuse. Such substances could be new chemical compounds, drug products, or peptides. Currently there are several ligands available through the NIDA drug supply system such as SR 141716A, SR144528, CP 55,840, anandamide, epibatidine, Kaffiralin 1 and 2, etc. All probes for cannabinoids, neuropeptides, nicotinic acetylcholinergic receptors and related

probes for drug abuse study are encouraged. In addition applications on biological screening of such new compounds as potential ligands for drug abuse research will also be considered.

Kristopher Bough, PhD
301-443-9800
Email: boughk@mail.nih.gov

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.

Kristopher Bough, PhD
301-443-9800
Email: boughk@mail.nih.gov

Drug Discovery – Chemistry and Pharmaceutics. Within this area, NIDA supports research concerning 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 novel medications for treating SUDs.

Preclinical Drug Development. Within this area, NIDA 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. This 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.

Clinical Drug Development. Within this area, NIDA seeks to support the clinical development of compounds that have completed (or are nearing completion of) successful preclinical evaluation of a novel pharmacotherapeutic- or immunological treatment(s) for persons with SUDs. Products can be evaluated in any Phase of clinical development, I, II, or III. Treatments should aim to help subjects become drug free, mitigate drug use, prolong abstinence/reduce craving, and/or facilitate survival from

drug overdose. Whereas it is expected that all clinical trials testing a novel medication will provide a behavioral therapy component, the scope of this funding announcement does not provide for the evaluation of the safety and/or efficacy of psychosocial interventions.

Therapies that a small business might consider developing include, but are not limited to:

- Repurposing of a compound developed for other indications (e.g., SSRIs, anti-epileptic drugs) that could be used to treat SUDs.
- A novel (e.g., NCE, novel drug formulation) that could be used to treat SUDs
- Vaccines for substances of abuse (e.g., cocaine, nicotine)
- Monoclonal antibodies for substances of abuse (e.g., methamphetamine, PCP)
- Naturally-occurring compounds (e.g., dietary supplements) that could be used to treat SUDs
- Or, a rationalized poly-therapeutic combination of pharmacotherapies designed to more comprehensively treat SUDs

Treatments that concurrently help alleviate associated psychiatric co-morbidities (e.g., depression, schizophrenia, PTSD, anxiety, etc.) and/or are focused upon underserved/vulnerable populations (e.g., pregnant women and their fetuses, adolescents, racial or ethnic minorities, women/gender issues, subjects within the criminal justice system) are also encouraged.

Also of special interest are products that incorporate technological advances to more efficiently develop novel therapeutics for SUDs, such as:

1. Improved methods to assess patient compliance during clinical trials (this can also include statistical modeling).
2. Improved adjuvants to boost antibody responses to drugs of abuse.
3. Discovery / development of biomarkers related to SUDs treatment outcomes. Because drug addiction is a brain disease which can change the structure and function of the brain, there is a unique opportunity to develop biomarkers that could reliably predict/assess SUD treatment outcome. To date, evaluations of SUDs often utilize subjective measures (e.g., patient-reported questionnaires) to assess disease progression and primary treatment outcomes. Biomarkers represent a more objective measure of physiological functioning that can be used to predict, diagnose, evaluate the progression of, and/or more accurately assess overall treatment safety and effectiveness. The goal of this initiative is to support the small business discovery/development of reproducible, quantitative biomarkers related to SUD treatment outcomes. Potential biomarkers might be derived from underlying variations in DNA, gene expression, proteins, metabolism, and/or neuroimages, among others. This solicitation is open to fast-track applications.
4. Improved methods that can predict oral bioavailability of drug-like substances (*in vitro; in vivo, in silico*). For example, this might include the development of an innovative test /device that can be used to help more effectively diagnose and/or manage patients with SUDs. The use of this novel diagnostic tool might help to: (a) expedite the development of-, and/or (b) enhance existing treatments for patients with SUDs. Possible diagnostic tests/devices that a small business might consider, but are not limited to, include:
    - An assay/device (e.g., skin sensors, oral swabs) that detects a substance of abuse more reliably than oft-used urinalysis. Optimally, the analytical test/device would be non-invasive and easy-to-use, such that it could be used on an outpatient basis.
    - Discovery/development of a diagnostic test/screen that could help physicians more effectively manage treatments for patients with SUDs.

Aidan Hampson, Ph.D.
301-443-8039

Email: aidan.hampson@nih.gov

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 information about areas of interest to the NIDCD, please visit our home page at http://www.nidcd.nih.gov/. Potential applicants are encouraged to contact the program staff listed in the following descriptions of NIDCD program areas early in the process of preparing the application.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NIDCD may decrease the length of an award and/or the budget recommended by a review committee, or not fund an application. According to statutory guidelines, total funding support (direct costs, indirect costs, fee) normally may not exceed $150,000 for Phase I awards and $1,000,000 for Phase II awards. With appropriate justification from the applicant, Congress will allow awards to exceed these amounts by up to 50% ($225,000 for Phase I and $1,500,000 for Phase II). Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting the application.

Phase IIB Competing Renewal Awards

The NIDCD will accept Phase IIB SBIR/STTR Competing Renewal grant applications to support research and development that are required to support the process of developing products that require approval by 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.

Research Topics of Interest to NIDCD

Hearing and Balance Program

Research and development related to lost auditory function. Development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new hearing aids, cochlear implants, and other assistive devices; development of systems designed to increase utilization of computers, telecommunication devices, or alerting systems by individuals with hearing impairments; development of improved screening technologies to assess hearing loss, especially in neonates and infants; development of new or improved batteries for hearing aids and or cochlear implants, including solar rechargeable devices; development of system on a chip technologies (e.g. DSP/VLSI/ASIC/FPGA) to provide self-fitting, self-adjusting, or other features that increase performance, accessibility, or affordability of hearing aids; development of better earmolds to address allergy, occlusion effect and/or feedback complaints; development of new outcome measures for assessing the efficacy of treatments for hearing disorders; development of technologies for the study, diagnosis and treatment of tinnitus including development of neural prostheses to treat specific neural deficits; 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.

Research and development related to lost vestibular function. Development of tests and treatments for balance disorders, particularly for the elderly; 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.

Development of new research tools to aid in the study of the auditory and/or balance systems including neuroimaging techniques (e.g. software tools, neuroanatomic tracer; optical and, multielectrode methods of assessing neural activity; new animal models of impaired function; diagnostic tools for inner ear function, including DNA-based assays and biochemical markers of disease. Development of improved tests and instruments for screening and diagnosis of inner ear function; development of technologies to enable gene transfer to the inner ear, including viral vectors; development of cell type specific markers and probes to examine cell lineage in inner ear regeneration; development of relevant software, including computational modeling tools, databases or web sites.

Roger L. Miller, Ph.D.
National Institute on Deafness and Other Communication Disorders
301-402-3458, Fax: 301-402-6251
Email: millerr@nidcd.nih.gov

Voice, Speech, and Language Programs

Research on voice, speech, and language disorders focuses on determining the nature, causes, treatment and prevention of communication 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; development of speech and language assessments and interventions for nonverbal autistic individuals; 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 speech impairment, including a brain computer interface (BCI) communication prosthesis; development of innovative treatment delivery systems or intervention protocols; design and development of diagnostic measures or materials for early identification of voice, speech and language impairment in children; development of assessments and treatments for childhood and adult voice, speech and 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 voice, speech and language.

Judith A. Cooper, Ph.D. [Language Program]
National Institute on Deafness and Other Communication Disorders
301-496-5061, Fax: 301-402-6251
Email: cooperj@nidcd.nih.gov

Lana Shekim, Ph.D. [Speech & Voice Program]
National Institute on Deafness and Other Communication Disorders
301-496-5061, Fax: 301-402-6251
Email: shekiml@nidcd.nih.gov

Taste and Smell Program

Research on the development of easily administered diagnostic tools for testing human chemosensory function in population studies; epidemiological studies of the prevalence of taste and smell disorders;

intervention strategies for smell and taste disorders; development of bitter taste-blockers targeted toward pharmaceuticals; the development of artificial sweeteners; influence of taste and smell haplotypes on chemosensory sensitivity; chemosensory stem cell biology; human pheromone detection; retronasal olfaction; high-throughput screening of putative chemosensory ligand-receptor interactions; olfactory biomarkers for neurodegenerative disease; chemosensory risk factors affecting diet and health; biosensors and electronic noses for medical and industrial applications; and the development of an inventory of chemicals at exceptional high purity.

Roger L. Miller, Ph.D.
National Institute on Deafness and Other Communication Disorders
301-402-3458, Fax: 301-402-6251
Email: millerr@nidcd.nih.gov

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

For additional information on research topics, contact:

Roger L. Miller, Ph.D.
National Institute on Deafness and Other Communication Disorders
301-402-3458, Fax: 301-402-6251
Email: millerr@nidcd.nih.gov

For administrative and business management questions, contact:

Mr. Christopher P. Myers
Grants Management Officer
National Institute on Deafness and Other Communication Disorders
301-435-0713, Fax: 301-402-1758
Email: myersc@nidcd.nih.gov

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.

NIDCR's small business programs are highly focused on maximizing translational science opportunities – moving rapidly and intentionally toward pushing innovation in basic orofacial biology into useful products. The following are areas of particular interest.

Special budgetary notice:

> For FY2014, NIH has received preapproval from SBA for select translational science topics that due to their complexity potentially could require budgets over the 50% statutory limits (greater than $225,000 for Phase I SBIR/STTR awards and greater than $1,500,000 for Phase II SBIR/STTR awards). The topics denoted below with a " ** " fall under this preapproval category. **However, before submitting an application to NIDCR for projects in these topic areas, applicants are strongly encouraged to contact their program official for guidance and instructions. Any budget request above these limits is expected to be fully justified and commensurate with the scope of work.**

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. Small business opportunities in this area include but are not limited to:

A. Develop early pregnancy genetic tests to screen fetal cells in maternal blood for genetic mutations involved in inherited syndrome and non-syndrome craniofacial defects.

B. Develop instrumentation to improve the diagnosis and treatment of inherited and acquired craniofacial defects.

C. 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, bacterial, and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations and malignancies of HIV infection and AIDS. Specific examples of technology development needs include but are not limited to:

A. 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.

B. Explore novel methods or agents to eradicate oral biofilms (dental plaque) on teeth, oral soft tissues, and dental implants without adversely affecting the normal oral flora.

C. 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).

D. Develop controlled release systems for local delivery of synthetic peptides, recombinant proteins, or other chemical or immunotherapeutic agents to prevent, control, and/or treat oral infectious diseases, or the oral manifestations of HIV infection.

E. 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.

F. Develop ways to interfere with microbial colonization and growth through the use of antimicrobial agents and chemotherapy.

G. Identify and exploit the structural features of oral biofilms for increased therapeutics delivery.

H. Develop computer programs and apply systems biology approaches to model biologically active peptide regions of oral components that have anti-fungal, anti-bacterial and anti-viral activities.

I. Develop substitutes of naturally occurring chemicals (phytochemicals) known to have a role in controlling opportunistic infections induced by HIV.

J. Develop synthetic peptides and recombinant proteins of oral components with anti-fungal, anti-bacterial and anti-viral activities including those against HIV and oral opportunistic pathogens.

**K. Develop oral topical formulations with combined microbicidal, analgesic, and anti-inflammatory activities to enhance oral mucosal defenses and prevent and/or control oral infections and lesions in HIV-infected and/or immunosuppressed subjects.

L. Discover, test, standardize, and validate novel biomarkers present in oral fluids for screening and clinical diagnosis of HIV, and oral opportunistic pathogens infections and AIDS malignancies. Apply similar strategies as listed below for oral, oropharyngeal and salivary gland cancers to AIDS malignancies.

Clinical Research

**A. Develop improved methods to detect and predict progression of dental caries, periodontal disease, reversible pulpitis and irreversible pulpitis.

**B. Improve or develop new methods to enhance oral and craniofacial surgery. This would include both intraoral and extraoral surgery.

**C. Develop improved methods to mechanically repair or treat tooth structure damaged by dental caries or periodontal disease.

Oral, Oropharyngeal and Salivary Gland Cancers

Emphasis is on molecular mechanisms of oral epithelial cell deregulation that lead to oral cancers. Research related to early detection, diagnosis, and prevention, and treatment of oral cancers is of particular interest. Examples include but are not limited to the following areas:

**A. Develop imaging techniques for the early detection, diagnosis and prognosis of pre-malignant lesions.

B. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant lesions in preclinical models.

C. Develop novel technologies for the genetic and molecular-targeted therapy (e.g. siRNAs, peptide based therapies) in preclinical models.

E. Develop regimens for the alleviation of the oral complications of cancer therapy.

F. Develop animal models to facilitate the testing of therapeutic and chemopreventive agents for oral cancers.

Temporomandibular Joint Disorder and Orofacial Pain

Emphasis on research for chronic disabling painful diseases of the oral-craniofacial-dental areas including chronic pain, neuropathies, and diseases of the temporomandibular joint. NIDCR encourages small business applications that include but are not limited to:

A. Developing improved techniques for measuring nociceptive, 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 orofacial treatments or interventions.

B. Developing improved biomarkers for neuropathic conditions affecting oral-craniofacial tissues or structures.

C. Developing assays facilitating reliable evaluations of relationships between biological and other risk factors as they relate to onset, and exacerbation of pain and for examining the transition from acute pain to chronic pain conditions.

D. **Discovering and developing novel, pharmacological medications for treating chronic orofacial pain disorders, by leveraging results from ongoing genetic studies of chronic pain conditions.

Saliva, Salivary Diagnostics, and Salivary Gland Diseases

Emphasis is on salivary gland physiology and pathophysiology and in the repair and restoration of the damaged gland. Examples of small business applications include but are not limited to:

**A. Development of viral, non-viral and gene therapy-based approaches to address compromised salivary gland function. Development of cell and tissue-based strategies and technologies for restoration of damaged or destroyed salivary gland function.

**B. Development of novel compounds or materials that protect and preserve salivary glands from head and neck cancer irradiation therapy.

**C. Development of non-invasive methods for the determination of efficacy and safety of artificial saliva, sialogogues, and of their delivery vehicles used in addressing the diminution or lack of saliva (xerostomia) due to Sjögren's Syndrome or head and neck cancer irradiation therapy.

**D. Development of biomarker strategies and technologies for the identification of Sjögren's Syndrome in blood or saliva.

E. Discovery of biomarkers derived from oral fluids that are predictive of the onset, progression and recurrence of oral diseases and conditions, such as periodontal diseases, caries, and oral, oropharyngeal and salivary gland cancers.

F. Development of immunological strategies and immunotherapy-based approaches for addressing xerostomia from Sjögren's Syndrome.

G. Development of enhanced or novel tools for early detection of salivary gland cancers.

Biotechnology, Biomaterials, and Applications for Regeneration and Restoration of Oral, Dental and Craniofacial Tissues

Emphasis is placed on the development of a broad range of technologies targeted at regeneration and restoration of diseased and injured hard and soft tissues of the oral and craniofacial complex and on translating these applications to the clinic. Tissues of interest include craniofacial and alveolar bone, the periodontal ligament, TMJ bone and cartilage, oral mucosa, facial skeletal muscle, vasculature and peripheral nerve. Also of interest are multi-tissue composites and organs, such as vascularized and innervated bone and muscle, salivary gland, tooth, periodontium, bone-periodontal ligament-cementum interface and osteochondral complexes. Specific examples of relevant small business applications could include but are not limited to:

A. Development of technologies for design, fabrication, and manufacturing of biomimetic and biocompatible biomaterials and scaffolds, including nanomaterials and self-assembling nano-scaffolds, for tissue engineering and regenerative medicine applications. Development of hydroxyapatite or remineralization techniques need to include assessments demonstrating the ability to replicate the mechanical and physical properties of mineralized tissue such as dentin and enamel or bone.

B. Development of cell-based technologies, including stem cell-based technologies. These include, designing strategies for isolation, purification, scaled up production, standardization, comparison and quality control of stem and progenitor cells and their differentiated progenies, derivation of efficient and predictable methodologies for cellular reprogramming, and advancing technologies for reconstruction of stem cell niches for augmenting tissue regeneration.

C. Development of bioreactor systems to facilitate design, fabrication, and manufacturing of soft and hard tissues. Among their capabilities, these bioreactors may be able to mimic biophysical forces, such as mechanical and electrical forces that normally guide tissue morphogenesis *in vivo*.

D. Development of improved dental composite materials, including biomimetic and self-healing materials and adhesive sealants. These include but are not limited to materials to replace Bis-GMA

resin-based systems that are suitable for restoring crowns of posterior teeth and exposed roots of the teeth. Any novel dental composite restorative components or systems must include assessments in a physiologically relevant test system that mimics microbial and physicochemical conditions found in the oral cavity.

**E. Development of methods, materials, and devices for orthodontic, prosthetic, and craniofacial applications including those that can be used for craniofacial bone distraction, craniofacial reconstruction, healing, and scarless repair.

F. Development of artificial tissue and organ mimics that can be adapted to high-throughput formats for a broad range of screening applications, such as analysis of biomaterial and tissue function, drug efficacy and toxicology assays, biocompatibility assays, genetic screening and others.

G. Development of mathematical, computational, and bioinformatics approaches for modeling oral and craniofacial tissues and organ function and physiology to address needs of system biology, synthetic biology, and single cell analysis.

H. Development of novel biomolecules, including growth factors, cytokines, small molecules, siRNAs, and others for counteracting diseases and injuries of oral and craniofacial tissues and promoting their regeneration.

I. Development of advanced viral and non-viral based biomolecule delivery technologies that can precisely deliver and release therapeutic proteins, nucleic acids, small molecules, or combinations thereof with predictable temporal kinetics to target specific tissue sites.

**J. Development of imagining diagnostics to accelerate clinical implementation of reliable, reproducible, highly specific and sensitive diagnostic instruments for dental caries, cracked teeth, pulp vitality, bone quality, and periodontal diseases.

Clinical and Behavioral Research

Provides support for the development of evidence-based products related to behavioral and social aspects of oral health, oral health prevention or treatment interventions, and other patient-oriented aspects of oral health. This includes support for clinical trials and patient-oriented research to establish safety and initial efficacy of products. NIDCR is especially interested in applications that significantly improve oral health by: 1) being broadly applicable to many populations, 2) contributing to meaningful oral health improvements for a specific population, 3) expediting translation of research findings into oral health improvements, and/or 4) equipping oral health care providers, educators or researchers with tools to improve public oral health. Examples of studies of interest include, but are not limited to, the following:

A. 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 in a variety of settings, including naturalistic settings, within clinical trials, within oral health care delivery systems, etc.

B. Develop and test novel compliance and survey measures or tools to identify the underlying causes of insufficient preventive dentistry for specific underserved populations.

C. Develop, or adapt for use in a new population or setting, novel measures or methods for identifying individual, family, group, or other processes that explain oral health behavior.

**D. Develop and test for safety, efficacy, and/or effectiveness of measures or materials for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders.

E. Develop, or adapt for use in a new population or setting, oral health interventions utilizing technology to improve efficiency of delivery (e.g., management of chronic pain related to temporomandibular joint disorders, etc.).

F. Develop, or adapt for use in a new population or setting, interventions addressing health behaviors highly associated with oral health (e.g., tobacco, alcohol, and other drug use; management of diabetes, HIV infection, or other chronic illnesses; etc.).

G. Develop technologies or modules that utilize existing web-based platforms to improve preventive oral health hygiene for children and adolescents (e.g., social marketing via web-based interaction, virtual reality "worlds", "massively multiplayer online games", etc.).

H. Develop and test innovative methods for facilitating collaborations, referrals, and/or ongoing follow-ups between oral health professionals and other health care professionals.

I. Develop and test web-based training or other innovative approaches for oral health care professionals to accelerate accurate translation of new knowledge regarding oral diseases and their effective prevention or treatment into clinical or public health practice.

J. Develop and test the effectiveness of innovative teaching tools to inform oral health professionals or the public regarding oral cancer prevention and early detection. Develop and test for safety and efficacy methods for diagnosing caries, pulp vitality and / or periodontal diseases that utilize non-ionizing radiation.

K. Develop and test for safety and efficacy methods for diagnosing caries, pulp vitality and / or periodontal diseases that utilize non-ionizing radiation.

For additional information on research topics, contact:

R. Dwayne Lunsford, Ph.D.
Coordinator, SBIR/STTR Program
Director, Microbiology Program
Integrative Biology and Infectious Disease Branch
Division of Extramural Research
National Institute of Dental and Craniofacial Research-NIH
6701 Democracy Blvd., Rm. 626
Bethesda, MD 20892-4878
301-594-2421, Fax: 301-480-8319
Email: lunsfordr@nidcr.nih.gov

For administrative and business management questions, contact:

Ms. Diana Rutberg
Chief Grants Management Officer
National Institute of Dental and Craniofacial Research
6701 Democracy Blvd., Rm. 658
Bethesda, MD 20892-4878
301-594-4798, Fax: 301-480-3562
Email: rutbergd@mail.nih.gov

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.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, the NIDDK may not fund an application or may decrease the length of an award and/or the budget recommended by a review committee. For topics listed in APPENDIX A: National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations, the NIDDK generally will not fund Phase I applications greater than $300,000 total costs or project periods greater than 2 years; or Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years. For all other topics, the NIDDK does not generally fund Phase I applications greater than $225,000 total costs or project periods greater than 2 years; or Phase II applications greater than $1,500,000 total costs or project periods greater than 3 years. Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB Competing Renewal Awards

NIDDK will accept Phase IIB SBIR/STTR Competing Renewal grant applications (only) from NIDDK-supported Phase II awardees that propose 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 IIB Competing Renewal opportunity. These awards are intended to support completion of research needed to obtain an IND or IDE. Applicants must provide evidence that they have consulted formally with the FDA concerning the research needed for the development of a drug, biologic or medical device and that the proposed research will address these regulatory requirements. Such evidence should include FDA correspondence from a pre-IND meeting for an IND application or a pre-IDE meeting for an IDE application, and the status of the project in a timeline related to Federal regulatory approval processes.

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.

- 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.
- Clinical and toxicology studies in support of an Investigational New Drug Application to the FDA.
- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Final Progress Reports

As detailed in NOT-OD-12-152, the NIH has released new instructions for SBIR/STTR Final Progress Reports.

The NIDDK is interested in tracking the progress of the small business concerns it funds and the products they develop. Funding priority will be given to those small business concerns that show not only their ability to develop products but also their growth as a small business concern towards independence from the SBIR/STTR program.

Additional Programs and Services for NIDDK SBIR Awardees

The NIDDK encourages awardees to apply for the following free programs:

- Phase I: The NIH Niche Assessment Program (http://grants.nih.gov/grants/funding/nap.htm) provides awardees with an in depth market analysis for their technology.
- Phase II: The NIH Commercialization Assistance Program (http://grants.nih.gov/grants/funding/cap/index.htm) will assist awardees in transferring their products to the marketplace.

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, HORMONE REPLACEMENT, 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. NIDDK will give priority to research that has already progressed to an *in vivo* model or to be clinically tested.

B. Integration of glucose sensor and insulin delivery systems to create an artificial pancreas.

C. Development of improved insulin and other pancreatic hormone delivery methods or devices.

D. Development of novel insulin and glucagon formulations showing improved kinetics and stability

E. Development of novel and more accurate non-enzymatic based glucose detection technologies.

F. Develop telemedicine approaches that can be incorporated as components/and or adjuvants of an artificial pancreas for better diabetes self-management.

G. Development of technologies that may promote and facilitate adherence/compliance by users of glucose control devices

II. SCREENING TESTS, DIAGNOSTICS AND BIOLOGIC TOOLS:

A. Development of techniques or products useful for predicting, preventing or delaying progression of diabetes, including tests for identifying patients at risk, and methods of monitoring disease progression.

B. Development of diagnostic tools for diabetic foot ulcers. These tests could be used to determine the risk of developing a diabetic foot ulcer or used for choosing treatment strategies.

C. Development of diagnostic tools to measure the autonomic neuropathy that develops in people with diabetes.

D. Development of clinical measures of oxidative stress, advanced glycation end-products and chronic inflammation that result from diabetes.

E. High throughput - Point of care technologies (reliable, accurate, cost-effective, highly sensitive, standardized having rapid turnaround time) for autoantibody detection, T cell –subsets-auto-reactivity and other immune parameters for autoimmune diabetes diagnosis and follow-up.

F. Development of methods to measure changes in the immune status that may be used as markers to follow the immune-modulatory activity and beneficial effect (beta cell mass preservation, reduction of

inflammation at the target organ, etc) of biologic agents tested in clinical trials for the prevention and/or treatment of T1D.

G. 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.

H. Development and validation of surrogate markers to monitor disease progression and potential therapies for diabetic complications.

I. Development and validation of tools for use by health care providers/systems to improve diabetes care and prevention.

J. 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.

K. Point of care low cost /portable technologies for diabetes and pre-diabetes diagnosis.

L. Development of Innovative technologies to predict and prevent hypoglycemia.

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 or devices to prevent and treat diabetic foot ulcers.

C. Development of new therapies to correct the underlying metabolic defects that result from diabetes, such as reactive oxygen species production and glycation of proteins.

D. 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.

E. 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.

F. Development of methods utilizing replenishable cell sources, especially stem cells that produce functional islet like cells/tissues that can be successfully transplanted.

G. 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.

H. Development of educational or psychosocial approaches that increase adherence to recommended diabetes treatment regimens or that reduce co-morbidities and complications (e.g., depression or foot ulcers).

I. Development of novel technologies that may facilitate self -management of diabetes and adherence to treatment.

J. New implantable and easy to replace technologies that may mimic the beneficial effect of gastric bypass/bariatric surgery for the treatment of diabetes without the need of a major invasive surgical procedure.

Other Endocrine and Metabolic Disorders

K. 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.

L. Development of Selective Receptor Modulators (SRMs) with tissue specificity and profiles that provide beneficial effects without the side effects secondary to therapies based on naturally occurring hormones.

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.

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 and new genetic screening methods for detection of biomarkers for genetic predisposition to GI-relevant diseases, e.g., IBD, hemochromatosis, Wilson's disease.

B. Development of improved means for detecting Barrett’s esophagus.

C. Development of methods for gastrointestinal endoscopy without the need for sedation.

D. 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).

E. Development of novel antifibrotic therapies for progressive liver failure.

F. Development of agents that would protect the gut epithelium from the damage caused by chemotherapeutic agents.

G. Development of quantitative tests of hepatic “reserve” which would be of use, for example, in assessing the risk of surgery in patients with liver disease.

H. Development of agents to promote the repair of gut epithelium barrier function, e.g., as needed following chemotherapy.

I. Development of humanized monoclonal antibodies against HCV and HBV to be used for prevention of recurrent disease in liver transplant patients.

J. Development of surrogate markers and non-invasive imaging methods to quantitatively assess liver fibrosis, inflammation, and fat that accurately assesses progression in patient.

K. Development of a rapid, diagnostic test for biliary atresia.

L. Develop and validate therapeutic interventions for treatment and/or progression of pancreatitis and its complications.

N. Develop more accurate and useful approaches to the diagnosis of chronic pancreatitis by functional, radiologic, endoscopic, or pathologic/cytologic means.

O. Develop gastrointestinal endoscopic instruments that have improved visualization and therapeutic capabilities for detecting mucosal abnormalities and pathologies and providing improved interventional capabilities.

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. Development of non-invasive techniques to detect liver disease.

J. Development of non- or minimally-invasive devices/ techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.

K. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

L. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.

M. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.

N. Development of an economical, accurate, and fast test for glutens and gliadins in foods.

O. Development of humanized mouse models of multi-allelic diseases.

P. Development of measurements to quantitate phenotypic or metabolic markers of disease progression in animal models, thus reducing the numbers of animals needed.

Q. Identification of surrogate markers looking at the plasma/sera proteome or metabolome at different stages of digestive or liver disease.

R. Development of novel proteomic or metabolomic technologies designed to study digestive and liver diseases, and their complications.

S. Development of biomarkers or imaging methods that quantitatively measure hepatic regeneration.

T. Development of biomarkers that quantitatively assess the degree of cold and warm ischemia injury in donor liver organs.

III. NUTRITION, OBESITY, AND EATING DISORDERS

A. Development of more accurate methods for assessing overall nutritional status.

B. Development of a non-invasive breath or blood test to accurately measure dietary intake.

C. 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.

D. Development of safe drugs that inhibit appetite or increase energy expenditure.

E. New technologies for quantitative assessment of body composition.

Kidney, Urologic and Hematologic Diseases

The Division of Kidney, Urologic, and Hematologic Diseases supports research into basic mechanisms of the organ and tissue function, and the diseases of the kidney, urologic and hematologic systems. Projects are expected 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, prevention strategies, 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. Bioinformatics tools.

E. Flexible databases useful for designing organ-specific databases and web sites.

F. Techniques for visualizing RNA distribution within cells or tissues.

G. New methods to acquire material from archival samples.

II. APPLICATION OF PROTEOMICS AND METABOLOMICS TO KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES

A Identification of surrogate markers in the plasma or serum that correlate with acute or chronic kidney disease, urologic diseases of the prostate or bladder, or disregulation of iron metabolism or other hematologic diseases (not leukemia), such as hemoglobinopathies or thalassemia.

B. Identification or development of novel proteomic or metabolomic technologies designed to study kidney, urologic, or hematologic diseases.

III. 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, electrolyte metabolism, 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 with minimal inflammation.
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, implantable dialyzers).
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 and methods / agents to reduce hemodialysis or peritoneal dialysis catheter-related infections.
4. Studies on improved biomaterials for hemodialysis and peritoneal dialysis catheters to decrease the foreign body response, biofouling and bacterial biofilm formation.

F. Improved techniques for 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, and materials that decrease uretheral and bladder inflammation due to foreign body.

H. Development of improved renal imaging techniques, differential renal function assessments and diagnostic assessment of non-malignant parenchymal diseases.

I. Development of early diagnostic tools, preventative measures, and treatment modalities for acute kidney injury.

J. Identification of mediators of kidney injury 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 of serum factors released by damaged kidney cells.
3. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity.
4. Development of new biomarkers for early detection of kidney dysfunction, prediction of progression, and early indication of recovery.
5. Development of rapid, accurate, and cost effective means of quantifying urine albumin.

L. Development of new technology to improve and optimize data collection of real-time observations (e.g., biomarkers, diet, physical activity, vital signs, psychological parameters, environmental factors), reporting of patient outcomes, interventions and adherence (e.g., diet, medicine) for clinical studies.

IV. UROLOGY

A. Analyses of factors responsible for initiation, fluctuation and progression of symptoms of lower urinary tract dysfunction (LUTD) leading to the development of a diagnostic tool. Development of animal, computer, or in-vitro models for the study of benign prostatic hyperplasia (BPH).

B. Development of diagnostic modes to clinically non-invasively or minimal-invasively measure bladder obstruction before and after surgical or pharmaceutical intervention and/ or treatment devices for bladder outlet obstruction.

C. Prevention, diagnostic, or treatment modalities for urinary tract infections.

D. 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. Development of diagnostic device for biochemical profiling of stones either in-vitro or in-vivo.

E. Development of localization methods through imaging or non-invasive methods or instrumentation using minimally-invasive methods to access stones for therapy. Methods to directly improve access to difficult stones.

F. Development of additional therapeutic agents and methods for prevention and/or treatment of urolithiasis.

G. Development of more real-time diagnostic assessment of lower urinary tract function using non-invasive, remote or minimally invasive measures, which can include neuro-pharmacological/neuro-physiological assessments in urodynamics.

H. Objective and diagnostic measurement devices or methods for assessment of urinary voiding and storage disorders, including stress, urge, and mixed incontinence, both in adults and children.

I. Development of non-invasive or minimally invasive treatment methods or pharmacological for urinary incontinence and/or bladder instability.

J. Non-invasive or minimally invasive methods to diagnosis bladder inflammation or bladder epithelial and/ or bladder wall changes of non-cancerous origin.

K. Non-invasive, reduced or non-radiological diagnostic methods for evaluating vesico-ureteral reflux in children and infants.

L. Methods for determining inflammatory cytokines, histamines, or other factors in voided urine, as markers for lower urinary tract inflammatory processes or other urologic disorders, including chronic and acute urologic pain disorders.

M. Development of simple diagnostic kits for evaluating growth factors in urine in a clinical laboratory.

N. Development of new or enhanced methods to derive synthetic or semi-synthetic biological matrices or other tools to treat urologic disease and/or augment the functionality of urologic tissues and organs.

O. Studies on improved biomaterials for indwelling, urethral catheters to decrease foreign body response, biofouling, and bacterial biofilm formation.

V. 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, validating, and standardizing organ specific iron concentration measurements as 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.

M. Development and validation of a sensitive, specific, reproducible, quantitative, and clinically applicable assay method for measuring serum hepcidin levels, as well as cellular hepcidin and ferroportin expression levels.

N. Design and validation of novel therapeutic agents that modulate hepcidin and cellular ferroportin expression and/or activity *in vivo*.

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

For additional information on research topics, contact:

DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES

Dr. Guillermo Arreaza-Rubín
National Institute of Diabetes and Digestive and Kidney Diseases
301-594-4724
Email: ga96b@nih.gov

DIGESTIVE DISEASES AND NUTRITION

Ms. Christine Densmore
National Institute of Diabetes and Digestive and Kidney Diseases
301-402-8714
Email: densmorec@mail.nih.gov

KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES

Kidney

Dr. Marva Moxey-Mims
National Institute of Diabetes and Digestive and Kidney Diseases
301-594-7717
Email: mm726k@nih.gov

Urology

Dr. Ziya Kirkali
National Institute of Diabetes and Digestive and Kidney Diseases
301-594-7717
Email: kirkaliz@niddk.nih.gov

Hematology

Dr. Terry Bishop
National Institute of Diabetes and Digestive and Kidney Diseases
301-594-7726
Email: bishopt@mail.nih.gov

For administrative and business management questions, contact:

Ms. Pamela Love
National Institute of Diabetes and Digestive and Kidney Diseases
301-435-6198
Email: pl48m@nih.gov

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects human health and disease in order to promote healthier lives. NIEHS achieves its mission through a multidisciplinary biomedical research program, prevention and intervention efforts, and a communication strategy that encompasses training, education, technology transfer and community outreach. NIEHS supports research and training focused on the identification, assessment and mechanism of action, and improved understanding of 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.

Tools for Improved Exposure Assessment and Biological Response

The NIEHS strategic plan for 2012-2017 includes a major focus on enhancing our ability to quantify an individual's exposure and individualized responses to the exposures. The National Research Council recently issued a report," Exposure Science in the 21st Century: A Vision and a Strategy", which presents an expanded, integrated vision of exposure science - one that considers exposures from source to dose, over time and space, to multiple stressors (http://dels.nas.edu/Report/Exposure-Science-21st-Century/13507). The goal for 2014 is twofold: to develop new technology and assays to measure human exposure to multiple chemical agents that may lead to disease or dysfunction and to foster the integration

of exposure and biological response. The desired application of these technologies and assays is in community, population-based (epidemiological) studies 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 exposure to environmental agents and the impact of the exposures on human biology.

1. Technologies for Characterizing Biological Responses

NIEHS supports the development of new assays and biomarkers to characterize individual responses to environmental stressors (including air pollution components, pesticides, toxic metals, endocrine-disrupting compounds, and other industrial chemicals but not pathogens or lifestyle factors such as diet or physical activity). Although these stressors act through different specific mechanisms, many of these result in alterations of major biological pathways – oxidative stress, inflammation, DNA damage response, immune function, mitochondrial function and epigenetic regulation - which ultimately mediate the effects of the exposures on human health. For 2014, NIEHS seeks the development of methods to measure the alteration of these pathways on the individual level as an indicator of the biological response to that individual's exposures.

Examples include but are not limited to:

A. Plasma or serum-based markers using altered RNA or protein expression or altered metabolite profiles.
B. Markers developed in exhaled breath, buccal cells, or other easily accessible, non-invasive biological samples that characterize alterations in key pathways associated with environmental stressors
C. Urinary biomarkers for DNA adducts, metabolites, or other cellular markers

2. Technologies for Generating Precise Measurements of Exposures to Environmental Agents and Integration of Exposure and Response

The NIEHS supports the development of technologies and devices to generate precise measurements of both external (point of contact) and internal dose of individual environmental agents and or their metabolites in real time for both acute and chronic exposures. The emphasis is on developing the ability to analyze multiple exposures simultaneously and to integrate exposure with biological response at the molecular or physiological level. In addition, NIEHS is interested in the development of economical technologies and approaches for storing human biological samples for long periods for subsequent analyses of analytes or macromolecules. Methods to store dried blood spots, urine samples, etc. with low cost, minimum storage requirements, and minimal degradation of sample quality are needed.

Examples include but are not limited to:

A. Development of sensors for measuring the levels of toxicants in biospecimens easily obtained from an individual, such as finger prick of blood, buccal cells, hair, exhaled breath, meconium, or urine.

B. The development of integrated devices linking exposure at the point of contact, internal dose, and biological response.

Hazardous Substances Detection and Remediation Program

The NIEHS Superfund Research Program (SRP) is interested in applying biotechnology and bioengineering approaches to develop novel strategies to characterize, monitor, and remediate hazardous substances at contaminated sites. SRP encourages applicants to develop green / sustainable detection technologies and remediation approaches that improve energy efficiency and reduce waste generation. Examples include but are not limited to:

- Development of advanced technologies that allow for real-time, on-site monitoring such as nanotechnology–based sensors and probes, biosensors, self-contained miniaturized toxicity-screening kits and miniaturized analytical probes and data analysis tools.
- Development of non-targeted or multi-analyte field sampling tools or kits to preserve or stabilize environmental samples for later laboratory analysis; as well as products that allow for rapid sample clean-up/preparation for analysis of environmental samples (soil, surface water, groundwater, sediments, etc.).
    - Development of methods or devices to detect and measure vapor intrusion or to detect non-aqueous phase liquids (NAPLs) and dense non-aqueous phase liquids (DNAPLs) in the subsurface.
- Development of assays or devices to determine the extent to which a contaminant is bioavailable.
- Development of instruments to identify subsurface geological structures and hydro-geological configurations and to sample for the presence of contaminants in these structures.
- Development of novel technologies for in situ remediation of contaminated sediments, soils, and groundwater.
- Development of cost-effective devices to detect or remediate chemical mixtures in environmental media.
- Development of computational, geographical information system-based, or modeling products for predicting fate and transport of contaminants, rates of remediation, or for identifying contamination sources.
- Development of nano-enabled structures, electrochemical methods, photocatalytic processes, thermal treatments, or filtration-based methods of remediation.
- Development of bioremediation and phytoremediation technologies including the use of genetic engineering approaches; or the development and culturing/propagation of plants, bacterial strains, or fungal species optimized for bioremediation.
- Development of high throughput assays or toxicity screening products for use in ecological risk assessments.

SRP recognizes the important public health impact of detection or remediation technologies that are applicable to nonpoint-source air pollution and drinking water; however, a higher priority will be placed on remediation and detection technologies with a clear connection to sites impacted by hazardous substances.

Please see the SBIR/STTR webpage (http://www.niehs.nih.gov/funding/grants/mechanisms/sbir/) for application information as well as other SBIR/STTR opportunities within NIEHS.

Improved Test Systems for Prioritization and Safety Evaluation

The NIEHS is interested in: (1) developing, standardizing, and validating sensitive and specific innovative tests and integrated testing strategies that can reduce, refine, or replace animal use and that will provide improved predictivity, and potential cost and time savings compared to current 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); and (2) developing mid- and high-throughput screens and tests using phylogenetically lower animal species (e.g., insects, fish, worms) to evaluate mechanisms of toxicity to identify mechanisms of chemically-induced biological activity, prioritize chemicals for more extensive toxicological evaluation, and develop more predictive models of *in vivo* biological response. The proposed tests and strategies should use computational and/or biochemical models, cell/ tissue cultures, and/or animal models that are relevant to existing safety assessment databases and human experience, and that can be extrapolated to estimate risks to humans. The endpoints for these tests or assays should take advantage of the new technologies (e.g., genomics, transcriptomics, proteomics, metabolomics), novel endpoints (biomarkers) including

those that are non-invasive, and computational approaches such as bioinformatics and cheminformatics. Examples include but are not limited to:

A. Improved experimental and computational tools for *in vitro* to *in vivo* extrapolation of chemical/drug exposure across a range of assay types

- Screening methods (e.g., fluorescent/chemiluminescent) to determine free and protein-bound concentrations of large numbers of structurally diverse chemicals in various media/matrices to support 'normalization' of potencies across *in vitro* assay types and improve methods of *in vitro* to *in vivo* extrapolation to more quantitatively relate diverse sets of available data to exposure data.
- Screening models to assess/quantify various absorption/distribution/metabolism/excretion (ADME) properties of chemicals including but not limited to: gut absorption of chemicals, renal excretion, biliary excretion, hepatocyte uptake clearance, hepatocyte basolateral efflux transport, hepatic metabolic clearance.
- Computational approaches that predict and incorporate intracellular concentrations of chemicals within *in vitro* assay systems over a range of cell types (various cell lines, Caco-2 cultures, primary hepatocyte suspensions/cultures).
- Tools for cross-species and cross-strain extrapolations to better incorporate existing and emerging data of human relevance

B. *In vitro* model systems, integrated assay approaches and computational methods ranging over a spectrum of 'biological space' that offer improved physiological relevance, improved predictivities, and/or provide mechanistic data on chemically-induced biological perturbations

- Undifferentiated/ differentiated human/mammalian stem cell model systems
- Biochemical assays of new/emerging biological pathways that may be important for human response to xenobiotic exposures
- Incorporation of xenobiotic clearance pathways (e.g., uptake, efflux, and/or metabolism as appropriate to a given model system)
- Organotypic model systems/3D 'tissue' systems that include multiple cell types and replicate the anatomy and function of intact tissues (e.g., skin, kidney, lung, the gastro-intestinal track, brain) and incorporate as appropriate immunological function
- Disease models (e.g., inflammatory models)
- Multi-organ models (e.g., liver/gastro-intestinal track)
- Alternative assays and integrated strategies to assess dermal irritation, dermal absorption, dermal hypersensitivity phototoxicity, and ocular toxicity

C. Non-mammalian or invertebrate models for specific toxicities that utilize endpoints that are conserved across species so the results can be extrapolated to human risk.

D. Identification and validation of predictive biomarkers that can be used to obtain improved mechanistic information and/or serve as the basis for earlier endpoints in toxicological studies.

E. Improved methods for fixing and preserving tissues that maintain cellular structure for histopathology while minimizing degradation of nucleic acids (RNA, miRNA, DNA, methylated DNA) so that archival tissue blocks can be better used for molecular analysis. Alternatives or improvements to formalin fixation, paraffin embedding (FFPE) of tissues are sought for improved molecular or genome-wide analysis for better use of tissue archives.

Tools for Communication and Engagement in Research

As part of its Partnerships for Environmental Public Health (PEPH) Program, NIEHS is interested in developing tools that build capacity, improve environmental health literacy, and support citizen science endeavors. The audience for these tools may include community groups, health care and public health professionals, educators, and students of all ages. Products may include:

A. Mobile tools and applications. With the proliferation of mobile phone and tablet use, NIEHS encourages the development of applications and technology to:

   a. Educate and train individuals and groups on environmental health topics, and empower them to apply that knowledge to daily living.

   b. Enable community-based organizations to collect data to understand, demonstrate, and communicate how their neighborhoods or region are exposed to environmental contaminants and the dangers they impose.

B. Web-based applications and databases. NIEHS encourages the development of tools that could be used to link and integrate information and resources from multiple sites. The goal is to facilitate community groups, health care and public health professionals, educators, and students of all ages to easily search for desired environmental health information and resources.

C. Gaming approaches. The goal is to develop and improve understanding of environmental health concepts actively, at the audience member's own pace and ability.

D. Documentaries, short films, and television shows. Educational shows with accompanying discussion guides, lessons, or activities to facilitate broader use of the show (for example, Unnatural Causes).

Development of resources on subjects of particular interest include known or emerging environmental toxicants, risk communication, environmental justice, health disparities, cumulative exposures, windows of susceptibility, and gene-environment interactions.

Other Topics within the Mission of the Institute

For additional information on research topics, contact:

Dr. Daniel T. Shaughnessy
National Institute of Environmental Health Sciences
Division of Extramural Research and Training
POB 12233 (K3-12)
Research Triangle Park, NC 27709
(919) 541-2506, Fax: (919) 541-4606
Email: shaughn1@niehs.nih.gov

For information on the Hazardous Substances Detection and Remediation Program, contact:

Dr. Heather Henry
National Institute of Environmental Health Sciences
Division of Extramural Research and Training
POB 12233 (K3-12)
Research Triangle Park, NC 27709
(919) 541-5330, Fax: 919) 316-4606
Email: henryh@niehs.nih.gov

For administrative and business management questions, contact:

Ms. Pam Clark
National Institute of Environmental Health Sciences
Division of Extramural Research and Training
Grants Management Branch
POB 121233 (K3-11)
Research Triangle Park, NC 27709
(919) 541-7629, Fax: (919) 541-2860

Email: evans3@niehs.nih.gov

For express mail:

530 Davis Drive (K3-12)
Morrisville, NC 27560

NATIONAL EYE INSTITUTE (NEI)

The NEI supports research with respect to eye diseases, visual disorders, mechanisms of normal visual function, preservation of sight, and the special health problems and requirements of individuals with impaired vision. Applications for all areas of vision research are encouraged. Examples that may be of interest to small businesses are provided below, but this list is not meant to be exhaustive.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NEI may decrease the length of an award and/or the budget recommended by a review committee, or not fund an application. For topics listed in APPENDIX A: National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations, NEI does not generally fund Phase I applications greater than $300,000 total costs or project periods greater than 2 years; or Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years.

Phase IIB Competing Renewal Awards

The NEI will only accept SBIR Phase IIB Competing Renewal grant applications from Phase II SBIR awardees to continue the process of developing technologies that ultimately require federal regulatory approval or require extraordinary time and effort in the Research and Development phase. Such technologies include, but are not limited to, pharmacologic agents, biological products, and devices. These technologies should be clearly related to the mission of the NEI. This renewal grant should allow small businesses to reach a stage in the project where interest and investment by third parties is more likely. The Competing Renewal application must be a logical extension of a previously completed Phase II (R44) SBIR grant. NEI grantees seeking SBIR Phase IIB Competing Renewal funding must submit an application within a period no later than the first six receipt dates following expiration of the previous Phase II budget period. Budgets not to exceed $750,000 total costs per year and time periods up to two (2) years may be requested for this SBIR Phase IIB Competing Renewal opportunity.

Potential applicants are strongly advised to contact Dr. Jerome Wujek (contact information provided below) before beginning the process of putting an application together.

The following topics are meant for illustrative purposes only and are not exclusive of other appropriate activities.

General Research and Development Topics

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. This encompasses research and development of innovative enabling technologies in areas of genomics, proteomics and nanotechnology. More specific topics include drug and high throughput assays; drug delivery systems; gene therapy, cell-based therapy and regenerative medicine; development of *in vitro* and *in vivo* disease models; surgical devices and materials; telemedicine, mobile health, and health education; and design/fabrication of new or improved ophthalmic instruments for diagnosis and treatment of eye disorders.

Specific Research and Development Topics

RETINAL DISEASES

New therapeutic approaches for inflammatory and degenerative diseases and for inhibition of abnormal angiogenesis in the retina and choroid; Better methods of diagnosing and treating diabetic retinopathy and other vascular diseases; Non-invasive techniques for early diagnosis of macular degeneration and other retinal degenerative diseases; Instruments and procedures for improved surgical management of retinal detachments; Retinal prostheses to help restore visual function; Better methods for cell or tissue transplantation.

CORNEAL DISEASES

New diagnostic tools, therapeutic agents and drug delivery methods for the treatment of corneal injury, infection, dry eye, ocular pain, and other ocular surface disorders; New biomaterials for corneal prostheses and corneal transplants; Instruments and procedures for correcting the refractive power of the cornea and/or measuring the cornea's optical properties or other physiological properties.

LENS AND CATARACT

New approaches in the post-operative management of cataract surgery; New surgical instruments for cataract extraction and new biomaterials for replacement of the natural lens; Design/fabrication of accommodative intraocular lenses.

GLAUCOMA AND OPTIC NEUROPATHIES

New therapeutic agents, instruments, and procedures for the diagnosis and treatment of glaucoma; Non-invasive methods to measure changes in the optic nerve head and retinal fiber layer.

STRABISMUS, AMBLYOPIA, AND REFRACTIVE ERROR

New approaches to detect and treat strabismus, amblyopia, and myopia; New tools and techniques for vision screening; New or improved methods and materials for correcting the refractive power of the eye and/or measuring the eye's optical properties or other physiological properties; New materials and manufacturing processes for eyeglasses and contact lenses.

VISUAL IMPAIRMENT AND BLINDNESS

Instruments and methods to better specify, measure, and categorize residual visual function; New or improved devices, systems, or programs that meet the rehabilitative and everyday living needs of blind or visually-impaired persons.

Additional Information

The NEI's programs are described in more 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.

For more information on research topics, contact:

Jerome Wujek, Ph.D.
Research Resources Officer
Division of Extramural Research
National Eye Institute
Suite 1300, 5635 Fishers Lane

Bethesda, MD 20892
National Eye Institute
301-451-2020, Fax: 301-496-2297
Email: wujekjer@nei.nih.gov

For administrative and business management questions, contact:

Mr. William Darby
Grants Management Officer
Division of Extramural Research
National Eye Institute
Suite 1300, 5635 Fishers Lane
Bethesda, MD 20892
National Eye Institute
301-451-2020, Fax: 301-496-9997
Email: darbyw@nei.nih.gov

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, sepsis, wound healing, and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components. The four divisions 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

Division of Biomedical Technology, Bioinformatics, and Computational Biology

Division of Training, Workforce Development, and Diversity

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/About/ContactByArea.htm). It also includes links to program announcements that highlight NIGMS areas of special emphasis (http://www.nigms.nih.gov/Research). 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.

Limited Amount of Award

According to statutory guidelines, total funding support (direct costs, indirect costs, fee) normally may not exceed $150,000 for Phase I awards and $1,000,000 for Phase II awards. With appropriate justification from the applicant, Congress will allow awards to exceed these amounts by up to 50% ($225,000 for Phase I and $1,500,000 for Phase II, a hard cap). NIGMS will not accept applications with budget requests exceeding this hard cap with the exception of projects fitting within the list of SBA-approved topics for awards over the statuary budget limitations; the entire list for NIH (including NIGMS) may be found in Appendix A of this document, and the specific SBA-approved topics for NIGMS are in italics below. If considering a project with a budget exceeding the hard cap, applicants are strongly encouraged to contact NIGMS program officials prior to submission, and preferably earlier during application

preparation. In all cases, applicants should propose a budget that is reasonable and appropriate for completion of the research project.

Phase IIB Competing Renewal Awards

NIGMS will accept Phase IIB SBIR-only 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 such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards, particularly for instrumentation or durable medical equipment (DME) designs. This renewal grant should allow small businesses to get to reach 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 NIGMS. Budgets for this Phase IIB Competing Renewal opportunity must follow the guidelines for Phase II applications (described above). These awards are mainly (but not exclusively) intended to support completion of research needed to obtain an IND or IDE. If applicable, applicants must provide evidence that they have consulted formally with the FDA concerning the research needed for the development of a drug, biologic or medical device and that the proposed research will address these regulatory requirements. Such evidence should include FDA correspondence from a pre-IND meeting for an IND application or a pre-IDE meeting for an IDE application, and the status of the project in a timeline related to Federal regulatory approval processes.

Prospective applicants considering a Phase IIB Competing Renewal application are strongly encouraged to contact either the Program person of record for the Phase II award or NIH staff listed at the end of this NIGMS topics announcement. To assist NIGMS in planning for Phase IIB applications, it is helpful for prospective applicants to submit to the NIGMS SBIR/STTR Coordinator (listed below) a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Phase II grant number
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-14-XXX)

The letter is non-binding and does not enter into the review process.

It is anticipated that only a small number of NIGMS SBIR Phase II awards would be eligible for a Phase IIB Competing Renewal award.

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 applications 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, including membrane proteins, assemblies and complexes by, but not limited to, x-ray diffraction, electron diffraction, NMR and mass spectroscopy.*

E. Imaging probes and sensors, other reagents and methods, instrumentation, software for microscopy, spectroscopy, and single molecule analysis of molecules, cells, tissues, embryos and small model organisms. Technologies for applications of microscopy, spectroscopy and single molecule analysis in basic biomedical research, including but not limited to light, electron, X-ray and scanning probe microscopy and fluorescence, magnetic and electron paramagnetic spectroscopy. NOT included are small animal and preclinical imaging and high throughput platforms for diagnostic and clinical applications.

F. Computational methods for analysis, prediction, and improving methods for determination of macromolecular structures and structure-function relationships.

G. 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, 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 expression, probes).

D. *Development of probes for detection of human genetic polymorphisms, including disease genes.*

E. Development of improved procedures for cytogenetics and diagnostic array technology.

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 and birth defects.*

I. Development of quantitative approaches to the analysis of complex biological systems.

J. *Development of tools and technologies to detect and monitor complex human phenotypes or* traits.

K. Development of technology to derive and expand pluripotent cell populations from non-embryonic sources, for example, induced pluripotent stem cells (iPS).

L. Development of improved technology to scale up the growth of induced pluripotent stem cells in culture and to regulate their differentiation state

M. Development of markers, reagents and tools to characterize the unique properties of iPS cell lines and to distinguish them from adult stem cells and more differentiated cells.

N. Development of existing human embryonic stem cell lines and new or existing iPS cells as a model system for drug discovery.

O. 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.

P. Improvement in procedures (statistical, computational, laboratory) for the high- and medium-throughput analysis of gene expression patterns and regulatory networks.

Q. *Development or improvement of methods for high throughput detection of epigenomic changes.*

R. *Development* or improvement of methods for characterizing the metabolic interactions of complex communities of microorganisms particularly those involved in host-microbe interactions.

S. Development of improved or novel methodology for structure/function analysis of very large macromolecular complexes involved in transmission or expression of genetic material.

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 cell signaling molecules and signaling intermediates, particularly those related to G-protein coupled receptors. Research in the field of glycomics, especially tool and methods development for this emerging field. 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 on wound healing and tissue repair. Research on the causes and treatments for common complications of critically ill patients (sepsis, systemic inflammatory response syndrome, multiple organ failure), especially directed towards the role of the inflammatory and innate immune 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 chemical entities 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.*

B. Development of synthetic methodology to improve the efficiency (broadly defined) of discovery and production of bio-medically relevant compounds.

C. Development of enzymes, catalytic antibodies, ribozymes, artificial enzymes, and host molecules as drugs or synthetic tools.

D. *Isolation, characterization, and development of factors and strategies, methods, or treatments involved in tissue repair, wound healing, sepsis, and traumatic injury, emergency, peri-operative, or critical care conditions, and associated pain management.*

E. Improved systems for collection, processing, and analysis of real time physiological data from injured or critically ill patients. Application of systems biology or complexity theory approaches towards understanding the physiology of injured and critically ill organisms. Development of tools, software, algorithms, etc. needed to link clinical, demographic, physiological, genomic, proteomic or other datasets of injured or critically ill organisms.

F. Metabolomics/metabonomics of injury and/or critical illness.

G. Development of strategies, methods, or new technologies to improve the delivery, monitoring, safety and efficacy of anesthesia.

H. *Research to improve drug design and delivery.*

I. Research to improve drug bioavailability by improved understanding of factors that influence absorption, metabolism, transport, or clearance of therapeutics and underlying mechanisms. Application of pharmacokinetic and pharmaceutical principles to the study of large biomolecules, such as proteins, polypeptides, and oligonucleotides.

J. *Research to discover, detect, and understand the genetic basis of individual differences in drug responses (pharmacogenomics).*

K. *Development of novel in vivo and in vitro methods to predict the safety and toxicities of pharmacologic agents.*

L. Development of bioinformatic, mathematical, and/or computational approaches/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.

M. Development of ontologies and modules useful for combining and mining databases containing genotype and phenotype information in order to discover correlations for drug effects, either therapeutic or adverse.

N. *Development of methods and tools for the field of glycomics including but not limited to development of: specific glycan structural databases, methodologies for synthesis of robust glycan libraries, glycan labeling reagents and glycol-enzyme inhibitors, analytical tools for determining carbohydrate structure abs assessing its biological function.*

O. Development and application of methods and materials for the elucidation of membrane protein structures at or near atomic resolution.

P. Development of high-throughput methods for sequencing and re-sequencing of mitochondrial genes and relevant nuclear genes and for proteomic and/or functional profiling of mitochondria in diagnosis of mitochondrial diseases.

Q. 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.

R. 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.

S. 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.

T. Development of tools to characterize oxidative stress and oxidative stress related molecules (NO, peroxynitrite, hydrogen peroxide, lipoxidation products modified proteins, DNA modifications, etc.) including the extent and/or localization (by organ/tissue/cell/organelle) of oxidative stress.

Division of Biomedical Technology, Bioinformatics, and Computational Biology

This Division enables the development of research tools in two broad areas: (1) 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, optical or laser spectroscopies, X-ray absorption/diffraction/scattering, detectors, electron or confocal microscopies, electrophoresis and other separation techniques, bioreactors, centrifugation, and flow cytometry. (2) New or innovative tools and methods in bioinformatics and computational biology, including social, population,

and behavioral modeling research. Example areas that may be of interest to small businesses include, but are not limited to:

A. ***Technology for Systems Biology:*** Development of novel technologies for proteomics, glycomics, metabolomics, and other aspects of systems biology for discovery and clinical applications, (e.g., sample handling, separations, mass spectrometry, and computational tools for protein identification, data curation and mining, and for integrating genome variation, pathways and networks with biological function).

B. **Technology for Structural Biology:** *Development of detectors and cameras for studying the structures of biomolecules in the size range of peptides to cells, using synchrotron radiation and multiple types of microscopy and spectroscopy.*

C. ***Bioinformatics and Computational Biology:*** Development of information and communication technology from computer and other quantitative sciences in support of biomedical or behavioral research, that apply best practices and proven methods for software design, construction and implementation to promote adoption by a broad biomedical research community. These may include:

1. Development of tools and methods for the modeling, simulation or analysis of complex biological systems.
2. Development of tools and methods for behavioral and social modeling, including mobile and other computer technologies to collect and validate data or to implement more effective broad-based behavioral interventions.
3. Development and enhancement of databases and data formats for biomedical research activities.
4. Development of collaborative environments and technologies to translate Big Data to knowledge, including but not limited to development of knowledge environments, research commons, data and metadata curation methods, and tools that address data security and privacy issues.
5. Development of tools and methods to collect, interpret, analyze and visualize scientific data through integration and interoperability of different data types.
6. Design and development of software and hardware for improving the effectiveness of computational approaches in biomedical research.
7. Development of computational biology software packages for integrative analysis of biomedical data, especially ones relevant to genomics, imaging, and clinical data.

Division of Training, Workforce Development, and Diversity

Research toward development of products or services to market discoveries derived from a broad research base and for science literacy or research capacity, focusing at the post-high school level and beyond, and particularly to enhance diversity of the scientific workforce.

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

For additional information on research topics, contact:

NIGMS SBIR/STTR COORDINATOR

Scott Somers, Ph.D.
National Institute of General Medical Sciences
45 Center Drive, MSC 6200

Bethesda, MD 20897-6200
301-594-3827 Fax: 301-480-2802
Email: somerss@nigms.nih.gov

CELL BIOLOGY AND BIOPHYSICS

Charles Edmonds, Ph.D.
National Institute of General Medical Sciences
301-594-0828, Fax: 301-480-2004
Email: edmondsc@nigms.nih.gov

GENETICS AND DEVELOPMENTAL BIOLOGY

Stefan Maas, Ph.D.
National Institute of General Medical Sciences
301-594-0943, Fax: 301-480-2228
Email: maassw@nigms.nih.gov

PHARMACOLOGY, PHYSIOLOGY, AND BIOLOGICAL CHEMISTRY

Pharmacology and Physiology
Alison Cole, Ph.D.
National institute of General Medical Sciences
301-594-3827, Fax: 301-480-2802
Email: colea@nigms.nih.gov

Biochemistry and Biorelated Chemistry
Pamela Marino, Ph. D.
National Institute of General Medical Sciences
301-594-3827, Fax : 301-480-2802
Email : marinop@nigms.nih.gov

BIOMEDICAL TECHNOLOGY, BIOINFORMATICS, AND COMPUTATIONAL BIOLOGY

Mary Ann Wu, Ph.D.
National Institute of General Medical Sciences
301-435-0787, Fax: 301-480-2802
Email: maryann.wu@nih.gov

TRAINING, WORKFORCE DEVELOPMENT, AND DIVERSITY

Fred Taylor, Ph.D.
National Institute of General Medical Sciences
301-595-3900, Fax: 301-480-2802
Email: taylorwf@mail.nih.gov

ADMINISTRATIVE AND BUSINESS MANAGEMENT QUESTIONS:

Ms. Patrice Molnar, M.A.
National Institute of General Medical Sciences
301-594-5136, Fax: 301-480-2554
Email: molnarp@nigms.nih.gov

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

For the most up-to-date information, please visit the NHLBI SBIR/STTR website (http://www.nhlbi.nih.gov/funding/sbir/index.htm) and subscribe to our listserv. You can also follow us on Twitter @NHLBI_SBIR

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. It also supports research on the clinical use of blood and all aspects of the management and safety of blood resources. The NHLBI SBIR/STTR program fosters basic, applied, and clinical research on all product and service development related to the mission of the NHLBI. The NHLBI has three extramural program divisions, described below.

Cardiovascular Sciences

The Division of Cardiovascular Sciences (DCVS) supports basic, clinical, population, and health services research on the causes, prevention, and treatment of cardiovascular diseases. The research programs of the Division encompass investigator-initiated research, targeted research, Institute-initiated research in targeted areas of research need and scientific opportunity, specialized centers of research focused on selected research topics, and clinical trials. Research supported by the Division is concerned with the etiology, pathogenesis, prevention, diagnosis, and treatment of coronary artery disease and atherothrombosis; structural heart disease; heart failure and arrhythmias; and hypertension and vascular diseases. A broad array of epidemiological studies is supported by the DCVS to describe disease and risk factor patterns in populations and to identify risk factors for disease. Also supported are clinical trials of interventions to prevent and treat disease; studies of genetic, behavioral, sociocultural, and environmental influences on disease risk and outcomes; and studies of the application of prevention and treatment strategies to determine how to improve clinical care and public health.

Lung Diseases

The Division of Lung Diseases (DLD) supports research on the causes, diagnosis, prevention, and treatment of lung diseases and sleep disorders. Research is funded through investigator-initiated and Institute-initiated grant programs and through contract programs in areas including asthma, bronchopulmonary dysplasia, chronic obstructive pulmonary disease, cystic fibrosis, respiratory neurobiology, sleep-disordered breathing, critical care and acute lung injury, developmental biology and pediatric pulmonary diseases, immunologic and fibrotic pulmonary disease, rare lung disorders, pulmonary vascular disease, and pulmonary complications of AIDS and tuberculosis.

Blood Diseases and Resources

The Division of Blood Diseases and Resources (DBDR) supports research on the causes, prevention, and treatment of nonmalignant blood diseases, including anemias, sickle cell disease, and thalassemia; premalignant processes such as myelodysplasia and myeloproliferative disorders; hemophilia and other abnormalities of hemostasis and thrombosis; and immune dysfunction. Research supported by the Division encompasses a broad spectrum of topics ranging from basic biology to medical management of blood diseases. The Division has a major responsibility for research to improve the adequacy and safety of the nation's blood supply. It also plays a leading role in transfusion medicine and blood banking, including research to evaluate blood donation screening, manufacturing, and processing technologies. The Division also has a major responsibility supporting research in hematopoiesis and stem cell biology and disease. It also supports hematopoietic stem cell transplantation research, and the application of stem cell biology findings to the development of new cell-based therapies to repair and regenerate human tissues and organs.

The NHLBI encourages applications through this Omnibus solicitation proposing innovative technologies related to any area within the NHLBI mission.

The NHLBI maintains a list of topics of unmet needs of particular interest (http://www.nhlbi.nih.gov/funding/sbir/funding/omnibus_grant_solicitation.htm) to the Institute. Special instructions for submitting applications in response to these topics are posted on the web page. The list is revised throughout the year, so please check regularly for updates. For more information, you can contact Kurt Marek, Ph.D. (301-443-8778 or kurt.marek@nih.gov) or the Division contact associated with your technology area listed at the end of the NHLBI section.

NHLBI-Supported Funding Opportunity Announcements (FOAs)

In addition to this Omnibus program announcement, the NHLBI releases targeted Funding Opportunity Announcements (FOAs) throughout the year.

These FOAs are listed to inform potential applicants about other funding opportunities to which they can apply; applications submitted in response to this Omnibus program announcement are not limited to research and development areas described in the following targeted FOAs. The NHLBI also encourages mission-aligned applications for innovative technologies outside these targeted areas.

(Funding Opportunity Announcements can be released or expire at any time throughout the year; please refer to the NHLBI SBIR/STTR web site for active announcements supported by NHLBI.)

1. NHLBI SBIR Phase IIB Bridge Awards to Accelerate the Commercialization of Technologies for Heart, Lung, Blood, and Sleep Disorders and Diseases (SBIR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-13-016.html
2. Small Market Awards: SBIR Phase IIB Competing Renewals for Heart, Lung, Blood and Sleep Technologies with Small Commercial Markets (SBIR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-012.html
3. SBIR Technology Transfer (SBIR): http://grants.nih.gov/grants/guide/pa-files/PA-11-347.html
4. Development of a Microfluidic Platform for Blood Testing in Neonatal and Pediatric Patients SBIR (SBIR/STTR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-026.html
5. Technologies To Assess Sleep Health Status in Populations (SBIR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-013.html
6. Onsite Tools and Technologies for Heart, Lung, and Blood Clinical Research Point-of-Care (SBIR/STTR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-011.html
7. Developing a Point-of-Care Device for the Diagnosis of Sickle Cell Disease in Low Resource Settings (SBIR): http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-010.html
8. Development of Highly Innovative Tools and Technology for Analysis of Single Cells (SBIR): http://grants.nih.gov/grants/guide/pa-files/PA-13-140.html
9. Safe and Effective Instruments and Devices for Use in Neonatal and Pediatric Care Settings (SBIR/STTR): http://grants.nih.gov/grants/guide/pa-files/PAR-13-090.html
10. New Technologies for Viral Hepatitis (SBIR/STTR): http://grants.nih.gov/grants/guide/pa-files/PA-12-090.html
11. New Technology for Proteomics and Glycomics (SBIR/STTR): http://grants.nih.gov/grants/guide/pa-files/PA-11-214.html

SBIR Phase IIB Awards

The NHLBI does not accept applications for Phase IIB SBIR competing renewal awards through this Omnibus solicitation; however, the NHLBI offers Phase IIB opportunities through the NHLBI Bridge Award and the NHLBI Small Market Award using separate funding opportunity announcements (Bridge Award: **RFA-HL-13-016**; http://grants.nih.gov/grants/guide/rfa-files/rfa-hl-13-016.html. Small Market Award: **RFA-HL-14-012**; http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-14-012.html). The purpose of the NHLBI Bridge and Small Market Awards is to accelerate the transition of SBIR Phase II projects to the commercialization stage by promoting partnerships between SBIR Phase II awardees and third-party investors and/or strategic partners. The Small Market Award is designed to support technologies addressing rare diseases or pediatric populations. The Bridge and Small Market Awards encourage business relationships between applicant small business concerns and third-party investors/strategic partners who can provide substantial financing to help accelerate the commercialization of promising new products and technologies that were initiated with SBIR funding. In particular, applicants are expected to leverage their previous SBIR support, as well as the opportunity to compete for additional funding through the NHLBI Bridge Award or Small Market Award programs, to attract and negotiate third-party financing needed to advance a product or technology toward commercialization.

Budgets up to $1 million in total costs per year and project periods up to three years (a total of $3 million over three years) may be requested. Development efforts may include preclinical R&D, which is needed for regulatory filings (e.g., IND or IDE) and/or clinical trials.

An SBIR Bridge Award or Small Market application must represent a continuation of the research and development efforts performed under a previously funded SBIR Phase II award. The NHLBI welcomes applicants previously funded by any NIH Institute or Center or any other Federal agency, as long as the proposed work applies to the NHLBI mission. Applications may be predicated on a previously funded SBIR Phase II grant or contract award. Applicants with Phase II contracts or awards from another Federal agency must contact the NHLBI to ensure their application can be received.

Applicants are strongly encouraged to contact Kurt Marek, Ph.D., at 301-443-8778 or kurt.marek@nih.gov for additional information.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, the NHLBI may not fund an application or may decrease the length of an award and/or the budget recommended by a review committee. NIH has received a waiver from SBA, as authorized by statute, to exceed the statutory budget limitations of $225,000 for Phase I and $1,500,000 for Phase II for specific topics relevant to the NHLBI that can be found below. Generally, the NHLBI does not fund Phase I applications greater than $300,000 total costs or project periods greater than 2 years. In addition, the NHLBI does not generally fund Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years. **Applicants with budget questions or considering requesting a budget greater than these amounts are strongly encouraged to contact Kurt Marek, Ph.D. (kurt.marek@nih.gov) before submitting an application**.

NHLBI Topics for Awards over Statutory Budget Limitations

A. Biomedical technologies (medical devices, instruments, pharmaceuticals, drugs, therapeutics, vaccines, diagnostics and biologics) for heart, lung, blood, and sleep related diseases and disorders requiring Federal regulatory approval (FDA) or clearance to be commercialized.

B. Small and large animal testing of products of tissue engineering and regenerative medicine, drugs, medical devices, therapeutics, and biologics and studies involving *in vivo* animal experiments for heart, lung, blood, and sleep related diseases and disorders.

C. Clinical trials and other experiments involving human subjects for heart, lung, blood, and sleep related diseases and disorders.

D. Therapeutics (drugs, devices, or biologics) development for heart, lung, blood, and sleep related diseases and disorders.

E. Device development for heart, lung, blood, and sleep related diseases and disorders

F. Diagnostics development for heart, lung, blood, and sleep related diseases and disorders.

G. Investigation of biomarkers and biosignatures of heart, lung, blood, and sleep related diseases and disorders.

H. Technologies to enhance clinical research for heart, lung, blood, and sleep related diseases and disorders.

I. Advanced instrumentation and high throughput tools for biomedical research in heart, lung, blood, and sleep related diseases and disorders.

J. Tools and platforms to improve the dissemination and implementation of evidence-based interventions for heart, lung, blood, and sleep related diseases and disorders.

Final Progress Reports

As detailed in NOT-OD-12-152, the NIH has released new instructions for SBIR/STTR Final Progress Reports.

The NHLBI is interested in tracking the progress of the small business concerns it funds and the products they develop. Funding priority will be given to those small business concerns that show not only their ability to develop products but also their growth as a small business concern towards independence from the SBIR/STTR program.

Additional Programs and Services for NHLBI SBIR Awardees

The NHLBI offers free assistance to applicants and awardees developing technologies requiring regulatory approval. Please contact Chris Sasiela, Ph.D. at chris.sasiela@nih.gov for more information.

The NHLBI also offers free assistance to applicants and awardees regarding their commercialization and business plan development. Please contact Kurt Marek, Ph.D. at kurt.marek@nih.gov for more information.

The NHLBI encourages awardees to apply for the following free programs:

- Phase I: The NIH Niche Assessment Program (http://grants.nih.gov/grants/funding/nap.htm) provides awardees with an in depth market analysis for their technology.
- Phase II: The NIH Commercialization Assistance Program (http://grants.nih.gov/grants/funding/cap/index.htm) will assist awardees in transferring their products to the marketplace.

For additional information on research areas, please contact:

CARDIOVASCULAR SCIENCES

Albert Lee, Ph.D.
Division of Cardiovascular Sciences
Advanced Technologies and Surgery Branch

6701 Rockledge Drive, Room 8204
Bethesda, MD 20892-7940
301-435-0567, Fax: 301-480-1454
Email: albert.lee3@nih.gov

LUNG DISEASES AND SLEEP DISORDERS

Ann Rothgeb
Division of Lung Diseases
6701 Rockledge Drive
Bethesda, MD 20892-7952
301-435-0202, Fax: 301-480-3557
Email: ar31t@nih.gov

BLOOD DISEASES AND RESOURCES

Phyllis Mitchell
Division of Blood Diseases and Blood Resources
Transfusion Medicine and Cellular Therapeutics Branch
6701 Rockledge Drive, Room 9148
Bethesda, MD 20892-7950
301-435-0481, Fax: 301-480-0867
Email: pm154p@nih.gov

NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

The National Human Genome Research Institute (NHGRI) has been guided, since the inception of the Human Genome Project in 1990, by a sequential series of plans, each of which has been developed with considerable input from the scientific community. These plans have always laid out ambitious goals and measurable objectives to gauge progress. NHGRI initiated its most recent planning process in 2008 and concluded with the publication in February 2011 of its newest strategic plan, Charting a Course for Genomic Medicine from Base Pairs to Bedside (Nature, 10 February 2011; Volume 470). The phenomenal advances that have marked genomics and have allowed genomic applications to transform many important fields made it an opportune time for the Institute to take a new look at genomics and its future.

The purpose of this document is to provide information to investigators about the breadth of NHGRI's research interests as laid out in the 2011 strategic plan. When appropriate, NHGRI will publish Requests for Applications that will be used to stimulate research in specific areas, to fill gaps in research knowledge, or to generate community resources that will further the mission of genomics or ELSI research.

The following are areas of high interest for investigator-initiated applications; they are not listed in priority order.

Technology and Methods Development

Technology development in DNA sequencing and genotyping are examples of activities that have changed the nature of what scientific research questions are practical to address, have enabled new approaches, and have potentiated the development of new community resource data sets. Many areas of

critical importance to the realization of the genomics-based vision for biomedical research require continued technological and methodological developments before pilots and then large-scale approaches can be attempted. Accordingly, the NHGRI will continue to support the development of new, fundamental technologies in all areas of genomics. Important areas in which technology development applications would be responsive to this Program Announcement include (but are not limited to) analyses of gene expression, discovery and characterization of genetic variation; identification of the genetic contributions to health, disease, and drug response; statistical analytic methods for understanding human genomic variation and its relationship to health and disease; and chemical genomics. There is also continued interest in supporting technology development for the comprehensive discovery of functional elements in the human and model organism genomes, and new DNA sequencing technology. Many of these assays would benefit from the ability to work with very small amounts of starting material, to the limit of single cells, along with minimally-invasive human specimens that are easy to collect, handle, and store . As these technologies mature, emphasis should be on high throughput, cost-effective methods that consistently produce very high quality data.

The Institute is also interested in contributing selectively to the development of new and needed technology in related areas, such as proteomics and systems biology research, when NHGRI funding can be used to further a truly unique development that will have a significant impact on the field.

Bioinformatics

Genome databases are essential resources for the biological and biomedical research communities. The creation and maintenance of effective databases are as important a component of research funding as data generation. The NHGRI has been a primary source of support for several major genetics/genomics-oriented databases and will continue to foster technology improvements to develop effective methods for integrating, displaying, and providing access to genomic information. Projects addressing new database technologies to improve the utility of genome databases would be appropriate as applications.

Computational Biology

The NHGRI has supported the generation of many large-scale genomic data sets such as genome sequence, haplotype maps, transcriptome measurements, protein interactions, and functional elements. NHGRI encourages the development of new computational methods and tools to analyze these and other large datasets, and to extract useful biological information from them. Where possible, existing community data standards and methods for data exchange should be used in the development of these new methods and tools. Further information on programs related to genomic databases and computational biology is available at this web site: http://www.genome.gov/10001735.

The development of new sequencing technologies has dramatically increased the amount of data produced for genomics. NHGRI is interested in supporting new computational applications for the production and analysis of data from these new sequencing platforms. These applications would include better computational methods for storage, compression and transfer of large datasets by biomedical researchers along with better analysis methods to interpret these data and integrate with other data types. Methods that are fast and computationally efficient are highly desirable.

Some genomic data analysis and display tools have been developed that already are used in the community that would benefit from additional work to support broader dissemination, for example making them efficient, reliable, robust, well-documented, and well-supported. NHGRI will support projects to extend the support for these informatics tools to make them readily adopted by any biomedical research laboratory that wishes to use genomic technologies to address biological questions.

Genomic Medicine

This is an emerging discipline that applies genomic technologies, such as genome-wide association testing and sequencing, to population studies to identify gene regions, genes, or variants affecting common etiologically complex conditions and predict individual risk. It also investigates the value of applying genomic methods in clinical care for the diagnosis, treatment, and prevention of complex diseases. The research scope of Population Genomics at NHGRI includes: developing resources and statistical methods for observational studies and clinical trials incorporating advanced genomic technologies; conducting proof-of-principle studies that apply genomic technologies to particular conditions that can be generalized to a broader range of conditions (e.g., translating genomic information to clinical care); and developing research methods and infrastructure needed for future epidemiologic studies of genetic and environmental contribution to disease in the United States, including a large, prospective cohort study of genes and environment. For additional information about Genomic Medicine NHGRI, please visit this web site: http://www.genome.gov/2755079.

Ethical, Legal and Social Implications

NHGRI, through the ELSI Research Program supports research studies that examine issues and, where appropriate, develop policy options regarding the ethical, legal and social implications of genomics. These studies may focus on issues associated with genomic research, genomic medicine or broader societal effects of genomic information and technologies. More detailed information on specific ELSI research priorities within each of these broad areas is available on the ELSI Research priorities web site: http://www.genome.gov/27543732.

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/.

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. Mental disorders constitute an immense burden on the U.S. population, with major depression now the leading cause of disability in the U.S., and schizophrenia, bipolar disorder, and obsessive-compulsive disorder ranked among the ten leading causes of disability. NIMH also takes a leading role in understanding the impact of behavior on HIV transmission and pathogenesis, and in developing effective behavioral preventive interventions. The NIMH conducts a wide range of research, research training, research capacity development, as well as public information outreach and dissemination to fulfill its mission.

For the Institute to continue fulfilling this vital public health mission, it must foster innovative thinking and ensure that a full array of novel scientific perspectives are used to further discovery in the evolving science of brain, behavior, and experience. In this way, breakthroughs in science can become breakthroughs for all people with mental illnesses.

The NIMH SBIR/STTR programs support small businesses to develop technologies that can advance the mission of the Institute, including in basic neuroscience research relevant to mental disorders, translational and clinical research of mental disorders, clinical diagnosis or treatment of mental disorders,

and dissemination of evidence-based mental health care. The NIMH Strategic Plan (http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml) and the National Advisory Mental Health Council's workgroup report "From Discovery to Cure" http://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/fromdiscoverytocure.pdf present key scientific priorities across these domains, and describe the need for tools to realize these priorities. Research priorities for the NIMH further include aspects of HIV/AIDS prevention, treatment, and care, in accordance with the Trans-NIH Plan for HIV-Related Research (http://www.oar.nih.gov/strategicplan/).

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

Also visit the NIMH SBIR/STTR home page: http://www.nimh.nih.gov/research-funding/small-business/index.shtml.

Important notes:

1. It is very helpful for potential SBIR/STTR applicants to contact NIMH prior to submitting an application, to ensure the application is of priority/interest to NIMH. Please see the contacts section.
2. An additional criteria that the federal government considers in supporting a small business with SBIR funds, is past commercialization performance. It is expected that small businesses who have received previous SBIR grants, have had success in commercializing their previously supported technologies. Small businesses that are mostly interested in research and development (and not commercialization) should consider other grant mechanisms at NIH, rather than the SBIR program. Program staff at NIMH can help identify the most appropriate grant mechanism to use.
3. The NIH has received a waiver from the SBA, regarding the funding cap. The technology areas that are included in this waiver can be found in the topic list located in Appendix A of this document. The technologies listed in the Appendix A (under NIMH) are of priority to this institute.

Phase IIB Competing Renewal Awards

The NIMH will accept Phase IIB SBIR Competing Renewal grant applications in two categories: 1) to continue research and development of technologies that ultimately require federal regulatory approval, and 2) to continue research and development of complex instrumentation, clinical research tools, or behavioral interventions and treatments.

Technologies in the former category (those that ultimately require federal regulatory approval) include, but are not limited to: pharmacologic agents and drugs, biological products, medical devices, vaccines, etc., related to the mission of the NIMH. Phase IIB SBIR Competing Renewal grants for such technologies should allow small businesses to get research and development to a stage where interest and investment by third parties is more likely.

Companies that are developing technologies that do not focus on drug development, but that require federal regulatory approval prior to commercialization, may be eligible to submit a Phase IIB Competing Renewal application.

For both technology areas, Phase IIB applications may be submitted through the Omnibus SBIR funding opportunity announcement. For this opportunity, budget limits of $3 million total costs and time periods up to 3 years may be requested. These budget allowances have been approved by the SBA through a waiver.

The following examples would make appropriate topics for proposed NIMH SBIR Phase IIB 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.
- 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.

Although technologies in the latter category listed above (complex instrumentation, clinical research tools, or behavioral interventions/treatments) may not require federal regulatory approval, extraordinary time and effort is needed for their research and development. Therefore, NIMH supports Phase IIB Competing Renewal awards of existing Phase II grants for such technologies. The Phase IIB Competing Renewal award for these would provide up to an additional three years of support at total cost funding levels of up to $$2.4 million for the project. These budget allowances have been approved by the SBA through a waiver.

Please contact the Program Director in the appropriate Division or Dr. Margaret Grabb (listed below) before beginning the process of putting an application together. In addition, prospective applicants are 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 (e.g. PA-11-133).

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 Phase IIB Competing Renewal grant.

Division of Neuroscience and Basic Behavioral Science (DNBBS)

The Division of Neuroscience and Basic Behavioral Science provides support for research programs in the areas of basic neuroscience, genetics, basic behavioral science, research training, resource development, technology development, drug discovery, and research dissemination. The Division has the responsibility, in cooperation with other components of the Institute and the research community, for ensuring that relevant basic science knowledge is generated and then harvested to create improved diagnosis, treatment, and prevention of mental and behavioral disorders.

In this Division, the SBIR and STTR programs support research and the development of tools related to basic brain and behavioral science, genetics, and drug discovery and development relevant to the mission of the NIMH. Such tools include: software (such as informatics tools and resources and tools for analyzing data); hardware (such as the development of instrumentation or devices); wetware (such as the use of iRNAs or other bioactive agents as research tools or molecular imaging agents or genetic

approaches to label neural circuits or modify circuit functions); and drug discovery related technologies such as high throughput screening (HTS) or computational pharmacology approaches.

AREAS OF EMPHASIS

- Novel imaging probes to study brain structure and function at all levels, from the molecular to the whole organ, using any imaging modality (PET, fMRI, optical, etc.).
- Drug discovery/drug development of novel compounds which act on molecular pathways (receptors, enzymes, second messengers, etc.) that are not typically targeted with currently available psychiatric drugs, and that have a strong biological justification as a novel mechanism for treatment of psychiatric disorders.
- Novel screening assays for high throughput acquisition and analysis of data about behavior and the brain, from the level of genes to the level of behavior.
- Novel technologies that would enable researchers to study how populations of neural cells work together within and between brain regions, in order to understand how changes in neural activity contributes to mental disorders.
- Develop informatics tools to facilitate the sharing of data between laboratories. This could include common data element efforts, but is not limited to that area.

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.

Division of Developmental Translational Research (DDTR)

The Division of Developmental Translational Research supports programs of research and research training with the ultimate goal of preventing and curing mental disorders that originate in childhood and adolescence. Relevant disorders include mood disorders, anxiety, schizophrenia, autism, ADHD, conduct disorder, eating disorders, obsessive compulsive disorder, and Tourette syndrome. The division stimulates and promotes an integrated program of research across basic behavioral/psychological processes, environmental processes, brain development, genetics, developmental psychopathology and therapeutic interventions. The mission of DDTR is to translate knowledge from basic science to discover the developmental origins of mental disorders and effect their prevention and cure.

In this Division, the SBIR and STTR programs support research and the development of technologies that can accomplish these goals in pediatric populations.

AREAS OF HIGH PRIORITY

- Develop, test and validate reliable and stable biomarkers that can identify at-risk individuals prior to disease onset, improve diagnosis, predict treatment response, or measure disease progression. Biomarkers are also needed in clinical trials to identify dose ranges, to identify a specific subpopulation of subjects to enroll in a treatment trial, or to measure efficacy or toxicity/side effects.
- Develop novel and targeted interventions (pharmacological, cognitive, behavioral, or device-based) that affect particular neural circuits and signaling pathways relevant to the developmental trajectory of the disease, and that have commercial potential.
- Based on expanded knowledge of neurobehavioral trajectories, develop novel objective assessment tools that can identify early signs of risk or onset of recurrence of particular mental

disorders or in domains of functioning (see MH's RDoC project: http://www.nimh.nih.gov/research-funding/rdoc/index.shtml) for pediatric populations.

- Develop computational behavioral assessment tools that can be used across ages, species, and cultures to evaluate dysfunction in domains relevant to mental disorders (e.g., mood dysregulation, deficits in executive function).

- Develop computational platforms to enable the integration and sharing of data characterizing typical and atypical developmental trajectories in humans and non-human animals.

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.

Division of Adult Translational Research and Treatment Development (DATR)

The Division of Adult Translational Research and Treatment Development plans, supports, and administers programs of research, research training, 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 research portfolio, which includes studies of the phenotypic characterization and risk factors for major psychiatric disorders; clinical neuroscience to elucidate etiology and pathophysiology of these disorders; and psychosocial, psychopharmacologic, and somatic treatment development. In addition, the Division supports an integrated program to clarify the psychopathology and underlying pathophysiology of psychiatric disorders of late life and to develop new treatments for these disorders.

In this Division, the SBIR and STTR Programs support research aimed at facilitating the validation and commercialization of new methods of assessing psychopathology and measuring treatment response to therapeutic agents. In addition, the SBIR and STTR Programs support the clinical development of novel pharmacologic treatments and technology development used to deliver novel psychosocial approaches to the treatment of mental illness in adults.

AREAS OF EMPHASIS

- Develop valid measures of the various constructs in the Research Domain Criteria (RDoC) matrix (see http://www.nimh.nih.gov/research-funding/rdoc/index.shtml), e.g., neurocognitive tasks, psychometrically sophisticated questionnaires, measures of behavior, and biomarkers, into a commercial product.

- Conduct early stage, proof of concept clinical trials to advance the development of novel therapeutics. The clinical trials are expected to include biological/behavioral data to assess target engagement and to help determine potential success or failure of the compound before moving on to larger clinical trials (see NOT-MH-11-015 http://grants.nih.gov/grants/guide/notice-files/NOT-MH-11-015.html).

- Develop, test and validate reliable and stable biomarkers that can identify at-risk individuals prior to disease onset, improve diagnosis, predict treatment response, or to measure disease progression. Biomarkers are also needed in clinical trials to identify dose ranges, to identify a specific subpopulation of subjects to enroll in a treatment trial, or to measure efficacy or toxicity/side effects.

- Develop clinical risk assessment instruments that encompass multiple domains (e.g., genetic, neurobiological, and environmental), are sensitive to developmental stage, and have high predictive power for the onset or recurrence of mental illness.

- Develop novel and targeted interventions (pharmacological, behavioral, or devices) that affect particular neural circuits and signaling pathways relevant to the developmental trajectory of the disease.
- Develop electronic sensors, monitoring devices and systems, and data analysis software for automated detection and diagnosis of mental disorders and key transdiagnostic dimensions of psychopathology.
- Develop risk assessment measures, methods and paradigms capable of evaluating individualized risk for developing mental disorders, or for developing particular benefits or harms during treatment for mental disorders, and communicating such probabilistic information to patients and their families in a readily understandable manner.

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.

Division of AIDS Research (DAR)

The NIMH DAR supports scientific research to understand and alleviate the consequences of HIV infection on the central nervous system, and research to strengthen the provision and outcomes of HIV/AIDS prevention and treatment. High-priority research areas for SBIR/STTR applications are described below.

- Develop and test novel, non-invasive diagnostic approaches (instrumentation, imaging, biomarkers, central nervous system [CNS] cell-based *in vitro* models) to detect neurocognitive dysfunction associated with HIV-1 infection and innovative technologies to study the mechanisms involved in HIV-1 associated neuropathogenesis and persistence of HIV-1 in the CNS. or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy
- Design and test novel therapeutic strategies aimed at amelioration of HIV-1 associated neurocognitive disorders (HAND) and eradication of HIV-1 from CNS reservoirs or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy.
- Discover and develop innovative technologies for targeting therapies to the brain, including antiretroviral drugs, nanotechnology, imaging tools to study HIV-aging interactions or HIV-related neurodegeneration and neuroprotective strategies with improved capability to cross the blood-brain barrier for amelioration of HAND.
- Design new strategies to reduce adverse effects of anti-retroviral drugs such as neuropsychiatric side effects and drug-drug interactions.
- Develop or adapt neurological/neuropsychological/neurobehavioral assessments to evaluate HIV-1 associated abnormalities in adults or children in resource poor environments that are adaptable to different cultures and languages.
- Develop innovative approaches to improve the scientific assessment of HIV sexual risk behavior through remote sensing devices, biomarkers, or other novel methods.
- Develop and test tools, curricula, and strategies that seek to reduce documented racial/ethnic, gender, and age-related disparities in HIV infection or in HIV treatment adherence and treatment outcomes.
- Develop novel tools and approaches to identify, recruit, enroll, and/or retain those most vulnerable to HIV/AIDS (e.g., African-American MSM, adolescents) in HIV prevention research and/or initiatives.

- Develop and test tools, curricula, or other approaches designed to facilitate the effective implementation of emerging biomedical HIV prevention methods (e.g., pre-exposure prophylaxis, microbicides, circumcision, etc.), including but not limited to approaches that address behavioral aspects of biomedical prevention (e.g., provider knowledge and training; patient uptake, adherence, HIV screening, and risk-reduction counseling; adverse event monitoring, etc.).

- Develop or adapt and evidence-based HIV sexual risk reduction, psychosocial coping, or treatment adherence interventions for delivery through the internet or mobile devices, with the aim of expanding intervention access, fidelity of delivery, and/or intervention tailoring.

- Develop novel tools and approaches designed to improve HIV treatment outcomes by rapidly linking individuals diagnosed with HIV to primary medical care, enhancing patient readiness for initiation of antiretroviral medications, improving and sustaining patient adherence to antiretroviral medications, and/or improving patient retention in medical care.

- Develop innovative approaches designed to improve the quality of HIV testing, (including rapid home based HIV antibody tests), HIV counseling, prevention, and treatment services by strengthening patient-provider communication and/or modifying the decision-making processes and practice behaviors of health care providers.

- Develop innovative approaches designed to improve the uptake and understanding of rapid home based HIV antibody tests by key populations at higher risk for HIV as well as innovative interventions that can be paired with home test kits to increase linkage and engagement in HIV care for those testing positive.

- Develop novel information technology tools designed to improve dissemination of evidence-based interventions and assist healthcare providers, community-based organizations, and professional or advocacy organizations in identifying, adopting, and implementing proven HIV prevention and treatment interventions.

Prospective applicants are strongly encouraged to contact Dr. Rebecca DelCarmen-Wiggins (listed below) with questions about the relevance of their interests to the mission of this division.

Division of Services and Intervention Research (DSIR)

The Division of Services and Intervention Research (DSIR) supports two critical areas of research:

- Intervention research to evaluate the effectiveness of pharmacologic, psychosocial, somatic, rehabilitative and combination interventions on mental and behavior disorders-including acute and longer-term therapeutic effects on functioning across domains for children, adolescents, and adults.

- Mental health services research to improve the access, cost, quality and outcomes of mental health care, as well as improve the dissemination and implementation of effective interventions in clinical and community settings.

The intervention research 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 treatment settings. Examples of areas of interest are:

- Randomized clinical trials evaluating the effectiveness of known efficacious interventions.

- Analyses of naturalistic databases to evaluate the effectiveness of known efficacious interventions.

- Identifying moderators and mediators of intervention effects as a step to design and test personalized interventions.
- Evaluating the combined or sequential use of interventions.
- Determining the optimal length of intervention, establishing the utility of continuation or maintenance treatment (that is, for prevention of relapse or recurrence).
- Evaluating the long-term impact of efficacious interventions on symptoms, functioning, and quality of life.

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.
- Enhanced capacity for conducting services research.
- The clinical epidemiology of mental disorders across all clinical and service settings.
- The dissemination and implementation of evidence-based interventions into service settings.

In this Division, the SBIR and STTR Programs support research and development of novel tools related to clinical trials (including preventive, treatment, and rehabilitative interventions alone and/or in combination), methodology, clinical epidemiology, services research, effectiveness research, health disparities (including rural populations) and the dissemination and implementation of evidence-based treatments/research into clinical and community settings in areas directly related to the mission of the NIMH. Such tools may include applied behavioral science and technology, software, hardware and associated technologies. Also supported is research and the development or adaptation of tools and technologies to be used to enhance the training and development of new generations of researchers and practitioners and to keep established researchers and practitioners up-to-date on the findings, implementation, and methods of interventions and services research.

Prospective applicants are strongly encouraged to contact Dr. Adam Haim (listed below) with questions about the relevance of their interests to the mission of this division.

Program Contacts

Margaret Grabb, Ph.D. (general questions about the NIMH SBIR program, Phase IIB program, DNBBS, DATR, DDTR divisional interests)
National Institute of Mental Health
6001 Executive Boulevard, Room 7201, MSC 9645
Bethesda, MD 20892-9645
Rockville, MD 20852 (for express/courier service)
Telephone: 301-443-3563
Fax: 301-443-1731
Email: mgrabb@mail.nih.gov

Adam Haim, Ph.D. (DSIR divisional interests)
Division of Services and Intervention Research
6001 Executive Boulevard

Room 7160, MSC 9649
Bethesda, MD 20892-9635
301-445-3593
Email: haima@mail.nih.gov

Rebecca DelCarmen-Wiggins, Ph.D. (DAR divisional interests)
Division of AIDS Research
6001 Executive Blvd., Room 6115, MSC 9619
Bethesda, MD 20892
Telephone: 301-443-3635
Email: rdelcarm@nih.gov

Gregory K. Farber, Ph.D. (general questions about technology development)
Director, Office of Technology Development and Coordination
6001 Executive Boulevard
Room 7162, MSC 9640
Bethesda, MD 20892
Telephone: 301-435-0778
Email: farberg@mail.nih.gov

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES (NIMHD)

The mission of NIMHD is to lead scientific research to improve minority health and eliminate health disparities. To accomplish this, NIMHD plans, reviews, coordinates, and evaluates all minority health and health disparities research and activities of the National Institutes of Health; conducts and supports research in minority health and health disparities; promotes and supports the training of a diverse research workforce; translates and disseminates research information; and fosters innovative collaborations and partnerships.

The Small Business Innovation Research (SBIR) Program and the Small Business Technology Transfer (STTR) Program enable the Nation's small businesses to apply their unique research and development capabilities toward accomplishing NIMHD's mission.

Through small business Phase I, Phase II, and Fast-track awards, NIMHD supports multi- and trans-disciplinary research and development leading to novel and or improved products capable of contributing to NIMHD's mission. Research and development may proceed and or be initiated at the molecular, cellular, individual, community or population level. Funding support for focus groups, phase I/II clinical trials, and other studies as needed to develop and test the proposed product may be requested. Additionally, NIMHD seeks innovative strategies that engage, collaborate, or partner with health disparity communities for designing and delivering innovative products and services to improve minority health and eliminate health disparities.

An overarching objective of NIMHD's investments in SBIR/STTR programs is to ensure that health disparity populations benefit equally from innovations in health promotion and prevention, biotechnology, imaging technologies, technologies for computational biology and informatics, including for example, systems, and structural biology; and technologies designed to advance personalized medicine, electronic health records and systems, etc. New or improved instruments, devices, and related methodologies to facilitate biomedical or behavioral research and efforts that seek to redesign or design new instruments, devices, and methods likely to increase access, reduce costs, and improve quality are of special interest.

Disparities in Health Outcomes

Disparities in health outcomes are believed to result from complex interactions between many 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. Innovations leading to improved health outcomes are of interest. 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 clinical settings;
3. Methodological and technological innovations that will integrate behavioral and social science with biomedical research, including gene related and environmental components;
4. Differential pharmacologic drug metabolism;
5. Impact of dietary decision making in diverse populations and effect on health disparity outcomes; and
6. Innovations in mobile health (mHealth) and telehealth/telemedicine technologies for communication, diagnosis, monitoring, evaluation, medical management, tracking, training, and treatment in underserved community settings and rural and remote locations.

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:

1. Efficacy of therapies in local populations;
2. Motivating positive behavioral changes in diverse populations;
3. Health outcomes related to health seeking, lifestyle, risk taking, protective behaviors and/or socioeconomic status;
4. Incorporating research into health promotion and disease prevention initiatives, applying new knowledge in a culturally appropriate manner in intervention/disease prevention initiatives;
5. Distribution of health structures and adverse health effects, and the sufficiency of healthcare frameworks in accommodating diverse social, cultural, political and economic factors; and
6. Development and/or refinement of culturally appropriate survey instruments, tools and databases to promote community based research engaging minorities, rural and other medically underserved populations; and culturally appropriate, evidence-based health promotion and disease prevention/intervention educational media such as software, videos, printed materials for health disparities populations and disadvantaged communities.

Innovations in Health Disparities Research

Studies that promote and advance evidence-based transformations 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:

1. Development of health disparity group-specific methodologies and diagnostics;
2. Development of technologies targeted for health disparity groups (i.e., gene chips, other novel assay systems, diagnostics, animal models, specialized instruments, etc.);
3. 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; and
4. Innovative technologies that enable use of electronic health record (EHR) systems and personal health records (PHR) for health disparities research. Elements could include interoperability and mapping among disparate technologies and data sets for multi-site interdisciplinary studies, innovations to enhance and accelerate participant recruitment for clinical studies, and security systems to protect storage and transmission of confidential medical data.

Development of Innovative Software and Tools for Science and Health Education

Funding support is available for the development of educational software and the application of educational technology and tools to facilitate learning of science or health science topics that target K-12 students, families, students from community, tribal, undergraduate colleges and the general public, including health service providers. Topics can range from basic biological, behavioral, social and physical sciences to specific human diseases, disorders, and conditions. Examples include but are not limited to obesity, nutrition, regenerative medicine, bioengineering, and how different parts of the body work across the lifespan, healthy living and lifestyle, mental health, health services research, health promotion, and disease prevention. Development of software, technology, or tools may be directed towards new products or adaptation of existing products designed to be more efficient, more accessible, cost-effective, more culturally appropriate, and user-friendly in promoting interactive learning, dissemination and promotion of health science to diverse populations. This effort is intended to yield efficient and user-friendly, culturally appropriate and effective educational units that can be extended to enhance the health science literacy of the general public or segments of the general public.

Examples of suitable topics include:

1. Web-based, stand-alone computational tools, instructional software or other interactive media for dissemination of science education;
2. Curriculum materials, Interactive teaching aids, models for classroom instruction, and teacher education workshops;
3. Development of health promotion and disease prevention/intervention materials such as informational videos and/or print materials and programs which are culturally appropriate for diverse populations and special communities;
4. Development and/or refinement of culturally appropriate survey instruments, tools and databases to promote community-based research engaging minorities, and rural and other medically underserved populations;
5. Development of methodologies, diagnostics, technologies, equipment, assay systems and portable devices that can be used in community settings, such as health centers, neighborhood clinics, doctors' offices, public schools, libraries, and rural and remote locations to facilitate biomedical and behavioral research;
6. Development of culturally appropriate educational materials for health promotion and disease prevention/intervention such as: software, videos, printed material to facilitate translation and dissemination of evidence-based health information; and

7. Innovative applications of health information technology, including telemedicine/telehealth tools and technologies, to facilitate electronic health information exchange, enable clinical research at the point of care, and improve access to quality health care for hard to reach populations.

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

For additional information on research topics, contact:

Mr. Vincent A. Thomas, Jr., MSW, MPA
Program Manager
National Institute on Minority Health and Health Disparities, NIH
6707 Democracy Blvd.
Suite 800, MSC 5465
Bethesda, MD 20892-5465
301-402-2516, Fax: 301-480-4049
Email: vt5e@nih.gov

For administrative and business management questions, contract:

Ms. Priscilla Grant, J.D., C.R.A.
Grants Management Officer
National Institute on Minority Health and Health Disparities, NIH
6707 Democracy Blvd.
Suite 800, MSC 5465
Bethesda, MD 20892-5465
301-594-8412, Fax: 301-480-4049
Email: pg38h@nih.gov

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 disorders such as stroke, epilepsy, Parkinson's disease, and autism are well-known. Many other neurological disorders are rare and known mostly to the individuals and families affected, their doctors, and scientists.

The NINDS SBIR/STTR program funds small business concerns to conduct innovative neuroscience research and/or development (R/R&D) that has both the potential for commercialization and public benefit. NINDS is committed to helping small business concerns commercialize their technologies through its grant funding, technical assistance program participation, and outreach at meetings. NINDS encourages all Phase II applicants to apply to the NIH Commercialization Assistance Program (CAP) to gain assistance in transferring their products to the marketplace. The CAP program is open to all Phase II grants that were active in the past five years. NINDS is increasingly tracking the progress of its funded small business concerns and the products they develop. Funding priority will be given to those small business concerns that show not only their ability to develop products but their growth as a small business concern towards independence from the SBIR/STTR program.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NINDS may decrease the length of an award and/or the budget recommended by a review committee, or not fund an application. According to statutory guidelines, total funding support (direct costs, indirect costs, fee) normally may not exceed $150,000 for

Phase I awards and $1,000,000 for Phase II awards. With appropriate justification from the applicant, Congress will allow awards to exceed these amounts by up to 50%. Applicants considering a requested budget greater than $225,000 for Phase I and $1,500,000 for Phase II (total funding support) are strongly encouraged to contact Stephanie Fertig (fertigs@ninds.nih.gov) before submitting an application.

NIH has received a waiver from SBA to exceed the hard cap for specific topics that can be found in APPENDIX A: National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations and only these specific topics can apply and receive awards over the hard cap. NINDS specific waiver topics are listed below. Generally, NINDS does not fund Phase I applications greater than $700,000 total funding support, with no more than $500,000 total cost in any year or project periods greater than 2 years. In addition, the NINDS does not generally fund Phase II applications greater than $3,000,000 total funding support, with no more than $1,500,000 total cost in any year, or project periods greater than 3 years. Again, applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application.

For all other funding opportunities, applications should follow the guidelines in the Award Budget section of those announcements carefully.

Phase IIB Competing Renewal Awards

NINDS only accepts Phase IIB SBIR/STTR Competing Renewal applications through specific opportunities that focus on the commercialization of SBIR and STTR developed technologies. These opportunities can be found on the NIH SBIR webpage: http://www.ninds.nih.gov/funding/small-business/small_business_funding_opportunities.htm. Contact Stephanie Fertig at 301-496-1779 or fertigs@ninds.nih.gov for additional information.

Research Topics of Interest to NINDS

General Areas of Interest

The NINDS accepts a broad range of small business applications that are significant, innovative, and relevant to its mission. Examples of research topics within the mission of NINDS are shown below. This list is not all inclusive and some research areas fall into multiple categories.

1. Therapeutics and Diagnostics Development for Neurological Disorders, including biomarker and diagnostic assays, therapeutics (drugs, biologics, and/or devices) for treatment of neurological disorders, and technologies/methodologies to deliver therapeutics to the nervous system.
2. Clinical and Rehabilitation Tools, including intraoperative technologies for neurosurgeons, rehabilitation devices and programs for neurological disorders, and brain monitoring systems
3. Technology and Tools, including technologies to image the nervous system, neural interfaces technologies, and tools for neuroscience research and drug development.

In addition to the research topics listed, NINDS also encourages applications in specific program areas. For additional information about NINDS funding opportunities, please visit our small business home page at: http://www.ninds.nih.gov/funding/small-business/.

Within the general areas of interest, the following specific topics fall under the SBA waiver and may require additional funds above the hard budget caps:

A. *In vivo* animal testing required for therapeutics and diagnostics development.

B. Drug and biologics preclinical discovery and development activities for regulatory submission, such as lead identification/optimization, preclinical efficacy testing, IND-enabling studies, and manufacturing for clinical trials.

C. Device preclinical discovery and development activities for regulatory submission, such as hardware prototyping, device/software verification, biocompatibility/sterilization testing, pre-clinical efficacy testing, large animal GLP safety testing, and preparing material/devices for human testing.

D. Clinical testing of therapeutics (drugs, devices, or biologics), diagnostics, clinical and rehabilitation tools (i.e. intraoperative technologies, rehabilitation devices and programs, and brain monitoring systems), and technologies for clinical research. This would include clinical research studies to test scientific hypothesis that are not feasible or practical to conduct in animal models but would inform a final device design.

E. *In vivo* animal testing of technologies for animal research and development of animal models for drug development and neuroscience research.

F. Research that requires special facilities to contain hazardous or infectious materials.

Clinical Trials

The NINDS is committed to identifying effective treatments for neurological disorders by supporting well-executed clinical trials. NINDS will not accept unsolicited SBIR/STTR applications that include clinical trials under the Omnibus solicitation. A clinical trial is a prospective biomedical or behavioral research study of human subjects designed to answer specific questions about safety, tolerability, efficacy and/or effectiveness of pharmacologic, behavioral, biologic, surgical, or device (invasive or non-invasive) interventions. This policy does not apply to (1) exploratory IND studies as defined by the FDA (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm078933.pdf) or (2) early feasibility studies of devices as defined by the FDA (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103.pdf).

NINDS accepts and supports SBIR and STTR clinical trial applications through specific opportunities, which can be found on the NINDS SBIR webpage: http://www.ninds.nih.gov/funding/small-business/small_business_funding_opportunities.htm. Other human subjects research can be submitted through the Omnibus solicitation and NINDS may decline funding of any application that includes human subjects for programmatic or administrative reasons. SBIR applicants considering projects involving human subjects research are strongly encouraged to contact Stephanie Fertig or Joanne Odenkirchen (contact information provided below) within the NINDS Office of Clinical Research.

Joanne Odenkirchen, M.P.H.
Clinical Research Project Manager, Office of Clinical Research
301-496-3104
Email: jo21x@nih.gov

Countermeasures Against Chemical Threats

NINDS manages the NIH Countermeasures Against Chemical Threats (CounterACT) program. CounterACT supports research and development on new and improved therapeutics or diagnostic technologies to prevent or mitigate the toxic effects from exposure to chemical threats, defined as toxic chemical agents that could be used in a terrorist attack against civilians, or those that could be released at toxic levels by accident or natural disaster. This includes the development of new (or support of existing) partnerships between small business and not-for-profit laboratories engaged in this research. The scope of research supported includes early screening for compounds with the desired biological activity, advanced preclinical and efficacy testing, through clinical research with promising candidate therapeutics. For more information on this program, including specific program announcements, please see: www.ninds.nih.gov/counteract. Applicants are strongly encouraged to consult with Dr. David Jett to determine the programmatic relevance of their proposed research.

David A. Jett, Ph.D.
Program Director, NIH CounterACT Research
301-496-6035
Email: jettd@ninds.nih.gov

For additional information on research topics, contact:

Ms. Stephanie Fertig, M.B.A.
Research Project Manager, Small Business Programs
301-496-1779, Fax: 301-402-1501
Email: fertigs@ninds.nih.gov

For administrative and business management questions, contact:

Ms. Tijuanna Decoster
Chief, Grants Management Branch
301-496-9231, Fax: 301-402-4370
Email: decostert@mail.nih.gov

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. Rapid advances in technology and genomic science, as well as significant changes in demographics and health care policies and practice, have placed pressing demands on nursing to find fresh approaches and interventions that improve health outcomes. 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.ninr.nih.gov/.

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 and mHealth 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.

L. Technologies and informatics-based solutions that promote health, including comprehensive high-throughput technologies.

M. Develop and creatively apply new and existing knowledge to the implementation of health information technology, including electronic health records.

N. Health care technologies to facilitate decision support, self-management, and access to health care.

O. Utilization of genetic and genomic technologies to advance knowledge of the “symptome,” including the biological underpinnings of symptoms associated with chronic illness.

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

A. ***Micro- and Nano-Systems, Platform Technologies.*** Development of BioMEMS, microfluidics and nanoscale technologies, including micro-total analysis systems, arrays, and biochips, for detection and quantitation of clinically relevant analytes in complex matrices. Application areas include biomedical research, clinical laboratory diagnostics, biodefense, high-throughput screening, drug delivery, tissue engineering, and implantable devices, among others.

B. ***Nanotechnology.*** Research and development of new enabling technologies for the fabrication and use of nanoscale components and systems in diagnostic and therapeutic applications. Examples include: development of new nanoscale patterning and manipulation systems; new approaches to the sensing and quantification of biologically important molecules using nanoscale specific properties; studies relating to the safety and commercialization of nanotechnology-enabled biomedical products.

For additional information on research topics, contact:

Dr. Paul Cotton
Program Director
National Institute of Nursing Research
301-402-6423, Fax: 301-480-8260
Email: Paul.Cotton@nih.gov

For administrative and business management questions, contact:

Mr. Brian Albertini
Chief, Grants and Contracts Management
National Institute of Nursing Research
Office of Grants and Contracts Management
6701 Democracy Boulevard, Room 710
One Democracy Plaza, MSC 4870
Bethesda, MD 20892-4870
(Courier delivery: Bethesda, MD 20817)
301-594-6869, Fax: 301-402-4502
Email: albertib2@mail.nih.gov

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS)

The mission of the National Center for Advancing Translational Sciences is to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. NCATS supports the small business Phase I, Phase II, Fast-track and Phase IIB Competing Renewal awards. For additional information, please visit our home page at http://www.ncats.nih.gov.

Limited Amount of Award

For budgetary, administrative, or programmatic reasons, NCATS may decide not to fund an application or may decrease the length of an award and/or the budget recommended by a review committee. Generally, NCATS will not fund Phase I applications greater than $225,000 total costs or project periods greater than 2 years; nor Phase II applications greater than $1,500,000 total costs or project periods greater than 3 years. For certain topical areas (Appendix A), the Small Business Administration has approved an NIH SBIR/STTR Topic Waiver list for which the NCATS generally will not fund Phase I applications greater than $325,000 total costs or project periods greater than 2 years; nor Phase II applications greater than $2,000,000 total costs or project periods greater than 3 years. Applicants considering a requested budget

greater than these limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB Competing Renewal Awards

Occasionally, NCATS may accept Phase IIB SBIR Competing Renewal grant applications to continue research and development of products that have a potential to address a prevalent bottleneck in the translational process, and where extraordinary time and effort is needed to reach a stage where interest and investment by third parties would be likely. Such products are expected to have a broad applicability, consistent with the mission of NCATS.

Topics of interest to NCATS

NCATS is interested in the development innovative tools, technologies, and intervention (drug, device, diagnostic) platforms that would support the creation of novel therapeutics and/or diagnostics, especially for rare and neglected diseases. The application may address any stage of translation, from target validation, through pre-clinical and clinical evaluation and intervention implementation and dissemination. Areas of current activity and interest are listed on the NCATS website and also include:

- Innovative platforms for identification and prioritization of targets for therapeutic intervention with clear clinical impact
- Technologies to determine alternative uses for existing therapeutic interventions
- Tools and technologies to allow assaying of activities of compounds on currently “non-druggable” targets
- Phenotypic assay development, including stem cell technology platforms for human “disease in a dish” applications and the evaluation of toxicity
- Co-crystallization high-throughput screening techniques
- Small molecule and biologics analytical characterization
- Tools and technologies that increase the predictivity or efficiency of medicinal chemistry, biologic, or other intervention optimization
- Accelerate bioengineering approaches to the development and clinical application of biomedical materials, devices, therapeutics, and/or diagnostics
- Protein-protein interaction assays for high throughput screening of rare disease related projects.
- Fluorescence probes to replace antibodies for determination of cellular protein translocation.
- Use of continuous flow manufacturing technology to address therapeutics shortages.
- Small autonomous devices for real-time detection of metabolites involved in metabolic and endocrine disorders
- Computational or web-based health research methods including
    - Platforms for generally applicable and scalable multi-disease registries and natural history studies
    - Clinical trials designs and analyses (e.g. for pragmatic clinical trials)
    - Use of patient data in comparative effectiveness studies and in identifying efficient interventions
- Tools and technologies that increase the efficiency of human subjects research, including development of technologies that facilitate rapid diagnosis and/or clinical trial recruitment and subject tracking, IRB evaluation, and/or regulatory processes
- Educational tools for clinical and translational research
- Novel platforms, technologies and tools to enable clinical and translational research, particularly those with mechanisms for inclusion of patient reported data
- Educational tools or materials for engaging communities to participate in research studies
- Mechanisms that improve dissemination and implementation of effective health interventions by physicians, patients, and public

- Increased efficiency of clinical research conduct including, but not limited to, regulatory decision support, appropriate study site selection, patient eligibility analysis, and recruitment tracking
- Searchable access to information about researchers and their expertise, including but not limited to their publications, published data sets, methods, patents, clinical trials, partnerships, collaborators, and clinical specialty/expertise (if applicable)
- Tools for meaningful sharing of research data with low barrier for provision and user friendly access
- User friendly mechanisms for voluntary donation by patients of their clinical data from their electronic medical record for research purposes
- Searchable access to information about research resources, facilities, methods, cells, genetic tests, molecules, biologic reagents, animals, assays, technologies with links to their use in published research studies

Other topics within the NCATS mission.

For additional information on research topics, please contact:

Ms. Lili M. Portilla, MPA
SBIR Program Manager
Phone: 301-217-2589, Fax: 301-480-3661
Email: Portilll@mail.nih.gov

For administrative, business management, and grant policy questions, please contact:

Mr. Long T. Nguyen
Grants Management Officer
Phone: 301-402-6737, Fax: 301-480-3777
Email: nguyen1@mail.nih.gov

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)

The mission of the National Center for Complementary and Alternative Medicine (NCCAM) is to define, through rigorous scientific investigation, the usefulness and safety of complementary and alternative medicine interventions and their roles in improving health and health care. For a detailed description of NCCAM mission, please see http://nccam.nih.gov/about/plans/2011/.

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 NCCAM Program Officers prior to submitting an application.

Topics of Interest to NCCAM

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. The areas of interest to NCCAM include but are not limited to development and validation of:

- technology for standardization and characterization of biologically active ingredients in natural products;
- technologies for taxonomic identification of botanical raw materials or detection of adulterants;

- methods for standardization and characterization of active components of mind-body medicine interventions;
- tools for the analysis of polysaccharides and polyphenols;
- botanical or botanically derived products with useful therapeutic potential including symptom management;
- technologies for the identification and characterization of bioactive metabolites derived from oral consumption of natural products;
- methods for the sustainable production of low yield natural products of commercial interest;
- biomarkers which correlate with efficacy of CAM therapies;
- standardized, reliable and economical tools that correlate with brain imaging in response to CAM treatment;
- technical imaging tools or instruments for studying manual therapies;
- CAM-based tools for pain management;
- tools, technology and instruments, including gaming technology, for the accurate assessment of adherence and/or fidelity to the use of CAM practices, interventions, and products;
- tools to improve patient-reported outcome measures of CAM clinical investigations;
- tools to improve biological and physiological outcome measures of CAM clinical investigations;
- tools to promote adoption of healthy behaviors through the use of CAM interventions;
- tools to assess the effects of CAM on healthy behaviors.

Topics That Are of Less Interest to NCCAM

The NCCAM Office of Communications is responsible for disseminating CAM information to the public. Therefore applications addressing software development or educational materials and courses (including Continuing Medical Education courses or CD's) will not be considered relevant to the NCCAM SBIR/STTR program. Also not eligible for support are applications seeking to develop cookbooks for special diets or instructional materials for clinical practice. NCCAM does not fund clinical practice other than as a component of funded clinical research.

Although applications to support the development of databases are not widely encouraged, these proposals will be considered if they are limited to aiding the taxonomic and phytochemical characterization of medicinal plants/fungi. Applicants are encouraged to contact the appropriate NCCAM Program Officer before submitting any SBIR proposals related to database development.

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

For additional information on research topics, please contact:

Dr. Craig Hopp
Program Officer
6707 Democracy Blvd.
Suite 401, MSC 5475
Bethesda, MD 20892-5475

301-496-5825, Fax: 301-480-1587
Email: hoppdc@mail.nih.gov

For administrative, business management, and grant policy questions, please contact:

Mr. George Tucker, M.B.A.
Grants Management Officer
6707 Democracy Blvd.
Suite 401, MSC 5475
Bethesda, MD 20892-5475
301-594-8853, Fax: 301-480-1552
Email: gt35v@nih.gov

NATIONAL LIBRARY OF MEDICINE (NLM)

The National Library of Medicine (NLM) offers support for research and development projects in biomedical informatics. NLM defines biomedical informatics as the science of optimal organization, management, presentation and utilization of information relevant to medicine and biology. The informatics projects of interest to NLM involve the application of computer and information sciences to information problems in a biomedical domain. For additional information about areas of interest to NLM and a listing of NLM funded applications, please visit http://www.nlm.nih.gov/ep. Business concerns interested in exploring SBIR/STTR grant opportunities with NLM are encouraged to contact the NLM representatives prior to submitting an application.

NLM's SBIR/STTR grant programs are focused on areas of particular interest from small business. The following narrative indicates the scope of projects suitable for the SBIR/STTR program that fit within the mission of NLM. They are not listed in priority order.

- New Technologies that facilitate utilization of electronic health records systems in clinical practice and public health
- Explore the use of social media to track disease outbreaks, pandemics, or assist patients in chronic disease management
- Tools for exploring climate and environmental effects on human health
- Tools and systems for applying research data to clinical problems
- Tools for disaster information management
- Tools and approaches for integrating large heterogeneous data sets

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

For additional information on research topics, contact:

Dr. Jane Ye
Program Officer
Division of Extramural Programs
National Library of Medicine
301-594-4882, Fax: 301-402-2952
Email: yej@mail.nih.gov

For administrative and business management questions, contact:

Mr. Dwight Mowery
Grants Management Officer
Extramural Programs Division
National Library of Medicine

301-496-4221, Fax: 301-402-0421
Email: moweryd@mail.nih.gov

DIVISION OF PROGRAM COORDINATION, PLANNING, AND STRATEGIC INITIATIVES (DPCPSI), OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS (ORIP)

ORIP supports high-quality, disease-free animal models and specialized animal research facilities to help meet the needs of biomedical researchers to understand, detect, treat, and prevent a wide range of human diseases. This support enables discoveries at molecular, cellular, and organ levels that lead to animal-based studies which then are translated to patient-oriented clinical research, aiming to find treatments to cure or ameliorate common and rare diseases. Through the small business Phase I, Phase II, Fast-track and Competing Renewal awards, ORIP is especially interested in funding research to develop biomedical methods and technologies that improve animal models of human diseases, and the care, use, and management of laboratory animals. ORIP also encourage the development and implementation of technologies to directly benefit the welfare of research animals and to directly improve animal facilities that support biomedical and behavioral research.

A list of some potential ORIP program topics follows the description of our Phase IIB Competing Renewal Awards. For additional information, please visit our home page at http://dpcpsi.nih.gov/ORIP/index.aspx.

Phase IIB Competing Renewal Awards

ORIP will accept Phase IIB SBIR Competing Renewal grant applications to continue research and development of methods, tools and devices for basic or translational research where extraordinary time and effort is needed for completion of these projects. The Phase IIB Competing Renewal award is intended to allow small businesses the opportunity to reach to a stage where interest and investment by third parties would be more likely. Such products are expected to have broad applicability, consistent with the mission of ORIP. Budgets that do not exceed $1 M per year in total costs (for up to 3 years), may be requested for this Phase IIB Competing Renewal opportunity; although it is expected that, in most cases, the requested budget would not exceed the final year budget of the applicant's previous Phase II award. This opportunity is available for the SBIR program only.

Please contact your Program Officer before beginning the process of preparing a Phase IIB Competing Renewal application. In addition, prospective applicants are strongly encouraged to submit to the Program Contact (listed above), 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 organizations
- Funding Opportunity Announcement Number (e.g., PA-12-XXX)

A letter of intent is not required, is not binding, and does not enter into the review of a subsequent application. It is expected that only a few of ORIP SBIR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

Research Topics of Interest to ORIP

RESEARCH AND DEVELOPMENT IN COMPARATIVE MEDICINE

A. Development of improved reagents and cost-effective methods to accurately screen and diagnose selected diseases of laboratory animal, and to perform overall assessments of animal quality and

health status. An urgent need currently exists for the development of improved methods for detection of active tuberculosis in nonhuman primates.

B. Development of improved reagents and techniques to isolate and propagate embryonic and somatic stem cells from laboratory animals. Improvement of the *in vitro* and *in vivo* methods to efficiently generate induced pluripotent stem cells and to reprogram the differentiated cells to other lineages.

C. Development of technology to identify molecular phenotype of a single stem cell or induced pluripotent stem cell from laboratory animals.

D. Development of improved reagents, techniques, and equipment for genomic and transcriptomic analysis and data -mining from tissue or cells of laboratory animals and animal models of human diseases.

E. Development of new technologies to rapidly phenotype large number of animals.

F. Development of technologies to identify biomarkers for clinical diagnostics in well validated disease models.

G. Development of vaccines and new therapeutic agents to prevent and/or control selected laboratory animal diseases. One high priority need is to develop methods to control and prevent Herpes virus B in nonhuman primates.

H. Development of commercially valuable reagents for lower organisms such as high-quality antibodies for use in zebrafish research.

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 and operational efficiency, including improvements in caging and remote monitoring in animal facilities.

K. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies of various human diseases, excluding most random mutagenesis projects performed on rodents. Applications primarily focused on cancer should typically be directed to NCI. A need exists for a small animal model of Hepatitis C virus infection in humans. Methods to produce genetically engineered mice susceptible to HCV replication, without the requirement for individual colonization with transplanted organs or cells in each experimental subject, are encouraged.

L. Identification, development, and characterization vertebrate animal models for studies of various human diseases and for use in training.

M. Development and refinement of high throughput technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.

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 to perform, analyze, capture and process data gathered in “omics” studies (genomics, transcriptomics, phenomics, proteomics, glycomics, epigenomics, metabolomics) in normal and disease-condition animal models.

P. Development of biological tools and reagents for reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease. Development of the technologies and procedures to test efficacy and safety of these experiments in animal models. Approaches to detect and track the implanted cells and tissues *in vivo*.

Q. Development of new technologies in animal /cell models to study the function (activation/silencing) of noncoding DNA or RNA regions in the development of diseases.

R. Development of *in vitro* animal cell culture techniques and computational methods to reduce the number of animals used in studies and replace certain tests conducted in animal models with new complementary methods.

S. Development of acellular biomaterials, biosensors and reagents to promote, detect and track reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease.

T Development of reagents, including antibodies, that will facilitate research using zebrafish as animal models of disease or for understanding basic aspects of development, physiology, or genetics.

Miguel Contreras, Ph.D.
Division of Comparative Medicine,
Office of Research Infrastructure Programs,
Division of Program Coordination, Planning and Strategic Initiatives ,
Office of the Director
Phone : 301-435-0744, Fax: 301-480-3819
Email: contre1@mail.nih.gov

RESEARCH AND DEVELOPMENT IN SCIENCE EDUCATION

Development of Innovative and Inquiry-Oriented Software and Gaming Resources for Science and Health Education

Funding opportunities are available for the development of discovery-oriented educational software and the application of educational technology and tools for health science topics that target K-12 students, families, students from community, tribal, undergraduate colleges and the general public. Topics can range from basic biological science to specific human diseases. Examples include; but are not limited to diet and exercise, infectious disease, bioengineering, the clinical trials process, how different parts of the body work across the lifespan, healthy living and lifestyle, mental health, and prevention of obesity, heart disease, diabetes, and other chronic diseases. Development of software, gaming technology, or other educational tools may be directed towards new products or adaptation of existing products designed to be more efficient, cost-effective, and user-friendly in promoting problem solving, interactive learning, dissemination and promotion of health science. This effort is intended to yield efficient and user-friendly, culturally appropriate and effective educational resources that can be extended to enhance the health science literacy and the health of the general public. A rigorous evaluation plan and broad dissemination are strongly encouraged.

Examples of responsive applications may include but are not limited to:

A. Web-based, stand-alone computational tools, instructional software or other interactive media for dissemination of science education;

B. Curriculum materials, Interactive teaching aids, models for classroom instruction, and teacher education workshops; and

C. Development of health promotion and disease prevention/intervention materials such as informational videos and/or print materials and programs which are culturally appropriate for populations and special communities.

Projects that target the following constituencies are strongly encouraged:

D. K-12 students, teachers and parents.

E. Students of community colleges, tribal colleges, undergraduate colleges and minority-serving institutions.

F. Patients and families with health conditions that disproportionately affect minorities and other medically underserved populations, including members of disadvantaged urban and rural communities.

Tony Beck, Ph.D.
Science Education Partnership Award (SEPA),
Office of Research Infrastructure Programs,
Division of Program Coordination, Planning, and Strategic Initiatives,
Office of the Director
Phone: 301-435-0805
Email: beckl@mail.nih.gov

OTHER RESEARCH TOPIC(S) WITHIN THE MISSION OF THE OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS

The Science Education Partnership Award (SEPA) program within the Office of the Director, ORIP supports and fosters health-related research and development projects designed to promote research career capacity at minority serving institutions and in underserved states, respectively. These programs support a wide variety of medical research, including workforce development tools to reduce health disparities experienced by disadvantaged groups and medically underserved populations. Applications involving partnerships with minority-serving institutions and the Institutional Development Awards (IDeA)-eligible institutions are strongly encouraged. Topics of special interest include:

A. Development and/or refinement of culturally appropriate survey instruments, tools and databases to promote community based research engaging minorities, rural and other medically **UNDERSERVED** populations;

B. Development of methodologies, diagnostics, technologies, equipment, assay systems and portable devices that can be used in community settings, such as health centers, neighborhood clinics, doctor offices, public schools, libraries, and rural and remote locations to facilitate biomedical and behavioral research;

C. Development of culturally appropriate educational materials for student, teacher and community health literacy and disease prevention/intervention such as: software, videos, printed material to facilitate translation and dissemination of evidence-based health information; and

D. Innovative applications of health information technology, including telemedicine/telehealth tools and technologies, to facilitate electronic health information exchange, enable clinical research at the point of care, and improve access to quality health care for hard to reach populations.

Tony Beck, Ph.D.
Science Education Partnership Award (SEPA),
Office of Research Infrastructure Programs,
Division of Program Coordination, Planning, and Strategic Initiatives,
Office of the Director
Phone: 301-435-0805
Email: beckl@mail.nih.gov

RESEARCH AND DEVELOPMENT IN CONSTRUCTION

The Division of Construction and Instruments supports the development and implementation of technologies to directly benefit the welfare of research animals and to directly improve animal facilities that support biomedical and behavioral research. In particular, the areas being supported include research on tools and equipment, their use to improve and ease care, and to facilitate monitoring of healthy animals. Another area of interest encompasses research to improve laboratory equipment to maintain the environmental conditions and to upkeep the infrastructure of animal facilities. Of special

importance is the employment of green technologies. Examples of topics of special interest include (but are not limited to) research leading to the development of better, more reliable, and more efficient:

A. Equipment such as vacuum cleaners, air filters, hoods, snorkels, autoclaves for animal research facilities, for barrier facilities, and other facilities with special needs and requirements;

B. Equipment to distribute water and food, and monitor their intake by research animals;

C. Equipment to monitor and protect the well-being of animals;

D. Equipment to increase the quality of life and prevent injuries of research animals;

E. Equipment to monitor and protect the well-being of animals;

F. Equipment and its use for maintenance of disease-free colonies;

G. Equipment to disinfect devices, furnishings, and other apparatus in animal facilities such as aquaria, cages, tunnels, and racks.

Research for the development of equipment and protocols for specific research needs is not within the scope of the ORIP mission.

Malgorzata Klosek, Ph.D.
Division of Construction and Instruments,
Office of Research Infrastructure Programs,
Division of Program Coordination, Planning, and Strategic initiatives,
Office of the Director
Phone: 301-435-2211
Email: klosekm@mail.nih.gov

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

CDC will accept SBIR grant applications on the April 5, August 5, and December 5, 2014 submission dates.

CDC's Mission: CDC works 24/7 to protect America from health, safety and security threats, both foreign and in the U.S. Whether diseases start at home or abroad, are chronic or acute, curable or preventable, human error or deliberate attack, CDC fights disease and supports communities and citizens to do the same.

CDC increases the health security of our nation. As the nation's health protection agency, CDC saves lives and protects people from health threats. To accomplish our mission, CDC conducts critical science and provides health information that protects our nation against expensive and dangerous health threats, and responds when these arise.

CDC Role:

Taking the health pulse of our nation
Detecting and responding to new and emerging health threats
Tackling the biggest health problems causing death and disability for Americans
Putting science and advanced technology into action to prevent disease
Promoting healthy and safe behaviors, communities and environment
Developing leaders and training the public health workforce, including disease detectives

Those functions are the backbone of CDC's mission. Each of CDC's component organizations undertakes these activities in conducting its specific programs. The steps needed to accomplish this mission are also based on scientific excellence, requiring well-trained public health practitioners and leaders dedicated to high standards of quality and ethical practice.

To keep pace with emerging public health challenges and to address the leading causes of death and disability, the CDC has begun an effort to quickly achieve measurable impact in a few targeted areas. The term "Winnable Battles" describes public health priorities with large-scale impact on health and with known, effective strategies to intervene. The charge under Winnable Battles is to identify optimal strategies and to rally resources and partnerships to accelerate a measurable impact on health.

CDC has identified these winnable battles based on the scope of the burden and our ability to make significant progress in improving outcomes. These priority areas include:

- Food Safety – Foodborne diseases affect millions of people and kill thousands in the U.S. each year.
- Global Immunization – CDC is implementing global immunization programs to eradicate polio, prevent measles and rubella, end the meningitis epidemic in Africa, accelerate the introduction of pneumococcal and rotavirus vaccines, and strengthen countries' own immunization systems.
- Healthcare-associated Infections – HAIs affect patient lives and add to our growing healthcare costs.
- HIV in the U.S. – There are more than 1 million people living with HIV in the U.S.
- Lymphatic Filariasis in the Americas – CDC and its partners are working to eliminate lymphatic filariasis (LF) from the areas of the Americas where the disease still exists.

- Mother-to-Child Transmission of HIV and Syphilis Globally – CDC works with Ministries of Health and other partners to prevent HIV and syphilis from passing from mothers to babies, thus reducing the number of babies who suffer early death and/or chronic illness caused by these infections.
- Motor Vehicle Injuries – Motor vehicle-related injuries are the leading cause of death in the first three decades of life.
- Nutrition, Physical Activity, and Obesity – Excess weight contributes to many of the leading causes of death in the United States, including heart disease, stroke, diabetes, and some types of cancer.
- Teen Pregnancy – In 2009, the number of births to teenage mothers was 409,840 – a birth rate of 39.1 per 1,000 women aged 15 to 19.
- Tobacco – Tobacco use remains the leading preventable cause of disease and death in the United States.

By identifying priority strategies and clear targets and by working closely with our public health partners, we can make significant progress in reducing health disparities and the overall health burden from these diseases and conditions.

In addition, CDC continues to focus on other high burden public health topics where it can make a significant impact in preventing illness, injury and disability and death. For additional information about CDC, please visit our home page at http://www.cdc.gov.

Questions of a general nature about the CDC SBIR program should be directed to:

Sean David Griffiths, MPH
Science Policy Advisor, Office of Science Quality
Office of the Associate Director for Science
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop D-72
Atlanta, GA 30333
404-639-4641; Fax: 404-639-4903
Email: SGriffiths@cdc.gov

or

Diana Bartlett, MPH, MPP
Health Scientist, Office of Technology and Innovation
Office of the Associate Director for Science, Office of the Director
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop D-72
Atlanta, GA 30333
404-639-4938; Fax: 404-639-4903
Email: DBartlett@cdc.gov

CENTER FOR GLOBAL HEALTH (CGH)

For additional information about CGH, please visit their web site at:
http://www.cdc.gov/globalhealth/index.html.

1. Development and Application of Reagent Drying System for HIV Drug Resistance Genotyping Reagent Kits

Background: A UNAIDS 2012 report indicates that scaling up of antiretroviral therapy (ART) in resource-limited settings (RLS) has significantly reduced HIV/AIDS-related morbidity and mortality and over 8.2 million of HIV-infected individuals were on ART by the end of 2011 in low- and middle-income countries. Due to the high genetic diversity of HIV virus and life-long treatment requirement of HIV infected individuals, emergence and transmission of resistant HIV is unavoidable. Data from studies conducted in RLS have shown that transmitted HIV drug resistance in those countries where ART scaling up initiated earlier is increasing and 80% of patients who were failing their ART acquired resistant HIV strains 12 months after ART initiations. Studies have also indicated that resistance to ART is a major cause of treatment failure in individuals with HIV infection and has been associated with higher mortality rates. To curb the emergence and transmission of resistant HIV, the World Health Organization (WHO) has developed a population-based public health approach strategy for prevention and monitoring of HIV drug resistance in RLS. However, implementation of the strategy has been hampered by the lack of laboratory infrastructure and cold chain transportation system for specimen and reagent transport.

The CDC International Laboratory Branch at the Division of Global HIV/AIDS has developed a broad sensitive and low cost HIV-1 genotyping assay (CDC HIV-1 PanGroup M genotyping Assay) based on the viral strains circulating in RLS. This assay has been successfully utilized to conduct HIV drug resistance surveillance and monitoring in eight U.S. President's Emergency Plan for AIDS Relief (PEPFAR) - supported countries using dried blood spot and plasma specimens. It has also been implemented in five national drug resistance laboratories for in-country support of HIV drug resistance surveillance and monitoring programs. Two of the five laboratories are designated by the WHO ResNet as National Drug Resistance Laboratories (NDRL) by using the CDC HIV-1 PanGroup M genotyping Assay. However, due to the constraint of transportation system of cold-chain-required reagents, the delivery of reagents has encountered many barriers as well as driving up the cost of HIV drug resistance surveillance program activities.

Specific Research Areas of Interest: The goal of this project is the development and application of liquid reagent drying system for CDC HIV-1 PanGroup M genotyping Assay reagents. The reagent drying system would allow to: (1) Dry the liquid reagents at room temperature (15-30°C) within 8 hours or less; (2) The reconstituted dried reagents with molecular reagent-grade water will have the same sensitivity and specificity as the conventional liquid reagents to reliably genotype HIV viral strains from HIV-1 infected individuals with an HIV-1 viral RNA level of 1,000 copies/ml of plasma or dried blood spot specimens measured by major commercially available Real-Time viral load kits, such as Abbott m2000 Real-Time HIV-1 viral load kits; (3). The dried reagents will have at least 6 months of shelf-life when they are stored at ambient temperature (10-45°C); (4) The HIV drug resistance genotyping profiles and pair-wise sequence analysis are identical and have ≥98% identical sequence score, respectively when the paired sequences are generated from specimens collected from ART-naïve or ART-experienced patients and tested with the reconstituted dried reagents and the conventional liquid reagents using Stanford HIV database drug resistance interpretation algorithms and routinely used sequence analysis software.

Impact and Commercialization Potential: A liquid drying system for CDC's HIV-1 PanGroup M genotyping Assay reagents would enable this assay and presumably others to be adopted more readily in RLS. Manufacturers of commercially available viral load kits may be interested in this drying system as a complementary component to their products.

For CGH programmatic information, contact:

Ron Ballard, Ph.D.
Associate Director for Laboratory Sciences
Center for Global Health
Centers for Disease Control and Prevention
1600 Clifton Road, Atlanta, GA 30333

Mail Stop D-69
404-639-2143, Fax: 404-639-7490
Email: RBallard@cdc.gov

For grants specific, administrative information, contact:

Ms. Angie Tuttle
Grants Management Officer
Procurement and Grants Office (PGO)
Centers for Disease Control and Prevention
2920 Brandywine Road
MS E-09
Atlanta, GA 30341-4146
770-488-2863
Fax: 770-488-2777
Email: ATuttle@cdc.gov

Mr. Hector Buitrago
Centers for Disease Control and Prevention
Procurement and Grants Office
2920 Brandywine Road
MS K-75
Atlanta, GA 30341-4146
770-488-2921
Fax: 770-488-2777
Email: HBuitrago@cdc.gov

Center For Surveillance, Epidemiology and Laboratory Services (CSELS)

Please visit their web site at: http://www.cdc.gov/ophss/csels/ .

2. Mobile Application(s) for Guiding Appropriate Laboratory Testing for New Anticoagulants

Background: Clinical laboratory tests are essential tools for clinical diagnosis and patient care. As science and technology progress, the number and complexity of clinical laboratory tests is rapidly expanding. This presents physicians with significant challenges in ordering diagnostic tests accurately and efficiently. The Clinical Laboratory Integration into Healthcare Collaborative (CLIHC)™ (a collaborative that came out of seven institutes on critical issues in clinical laboratory practice convened by CDC between 1984-2007) is addressing challenges clinicians face in selecting the appropriate clinical laboratory test. With more than 10 billion laboratory tests ordered annually, the adverse impact of incorrect test selection is a threat to patient care, patient safety, and costly to the healthcare system. Mobile applications are one clinical decision support tool solution to this challenge. Studies have estimated that roughly 80 percent of the nation's physicians are using smartphones and roughly one in three are using a tablet to help with healthcare decisions.

In 2012, the CLIHC™ subject matter experts (SMEs) and CDC developed and launched the *PTT Advisor* app. It provides physicians with a step-by-step interactive guide for appropriate follow-up testing for a patient presenting with a normal prothrombin time (PT) and an abnormal partial thromboplastin (PTT) result. These SMEs and CDC are now developing laboratory testing algorithms to guide physicians' use of new oral anticoagulants. Anticoagulants are the mainstay of therapy for the acute and long-term prevention and treatment of numerous coagulation related disorders and events. Across healthcare settings, anticoagulants have been consistently identified as the most common cause of adverse drug

events (ADEs). Physicians, and patients, will benefit from these step-by-step algorithms in mobile apps to guide appropriate laboratory testing for safe and effective anticoagulant use.

Specific Research Areas of Interest: The goal of this project is to design and develop an interactive mobile application(s) for smartphones, tablets, and other mobile devices to guide physicians' accurate clinical laboratory test selection for monitoring patients on anticoagulant drugs. The tool will guide physicians through sequential algorithms for appropriate test ordering. The app will also provide additional diagnostic and monitoring information. The development of the application should include small-scale pilot testing providing feedback from users and evaluation of the utility and effectiveness of the application. Appropriate laboratory testing will direct physicians in correct use of anticoagulants and improve patient care and safety.

- Create an innovative, useful mobile app product on both the Android and iOS operating systems that has demonstrated ability to improve patient care through better laboratory test selection and the possibility to reduce adverse drug events for patients on anticoagulant medications.
- Evaluate the mobile app based on feasibility, acceptability, ease-of-use and impact on the care of patients requiring anticoagulant drugs and make recommendations for how to improve the application based on the evaluation.

Impact and Commercialization Potential: Interactive mobile application(s) for smartphones, tablets, and other mobile devices would guide physicians' accurate clinical laboratory test selection for monitoring patients on anticoagulant drugs and would direct physicians in correct use of anticoagulants and improve patient care and safety. Hospital systems and physician groups would be the targeted consumers of the app.

Visit the CSELS homepage for more information on CSEL's research program areas
http://www.cdc.gov/ophss/csels/

For CSELS programmatic information, contact:

Sean David Griffiths, MPH
Science Policy Advisor, Office of Technology and Innovation
Office of the Associate Director for Science
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop D-72
Atlanta, GA 30333
404-639-4641; Fax: 404-639-4903
Email: SGriffiths@cdc.gov

For grants specific, administrative information, contact:

Ms. Devi Hawkins
Centers for Disease Control and Prevention
Procurement and Grants Office
Mail Stop K-69
2920 Brandywine Road
Atlanta, Georgia 30341
770-488-2543, Fax: 770-488-2670
Email: DHawkins@cdc.gov

NATIONAL CENTER ON BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES (NCBDDD)

For additional information about NCBDDD, please visit their web site at: http://www.cdc.gov/ncbddd.

3. Low Cost Technology for Small Rice Mill Micronutrient Fortification

Background: Micronutrient deficiencies account for an estimated 7.3% of the global burden of disease. Globally, it is estimated that as many as 4–5 billion people are iron deficient. Iron deficiency accounts for over half of anemia cases which, for pregnant women, can result in adverse birth outcomes. Further, an estimated 300,000 folate-preventable neural tube defects occur every year. Babies born with neural tube defects who survive past infancy face a lifetime of physical challenges and medical complications. Adequate consumption of other micronutrients, such as vitamin A and zinc can also help ensure optimal birth outcomes. One way to increase micronutrient consumption is through fortification of staple products such as wheat flour, corn flour, and rice. Folic acid fortification initiatives in the United States, Chile, Costa Rica, and South Africa, have been shown to result in a decreased prevalence of neural tube defects. Studies done in Brazil have shown vitamin A and iron fortification initiatives to be successful in increasing retinol and decreasing anemia, respectively.

Micronutrient fortification, however, cannot be successful unless the products of highest consumption are fortified. Globally, rice accounts for 20% of calories consumed. Almost 90% of rice is consumed in Asia, and consumption in Sub-Saharan Africa has risen by more than 50% in the past two decades. These two regions also account for the highest burden of micronutrient deficiencies globally. Fortifying rice in these two regions can help drastically reduce the global burden of micronutrient deficiencies. Although some countries currently fortify wheat flour, as of 2012, only 6 countries fortify rice.

A large number of small rice mills exist in many developing countries. These small mills provide rice on a community level as compared to larger mills that have broader population coverage. The cost for these small rice mills to integrate advanced fortification technologies into their current mills could make fortification impossible. However, if a technology was available that could be easily and cost-effectively integrated into existing small mill technologies, rice fortification for these small mills could be possible and provide them with a competitive advantage in the small mill market.

Specific Research Areas of Interest: The goal of this proposal is to develop a rice fortification technology aimed at use by small mills, which is less expensive but very effective in providing micronutrients to a population for the prevention of micronutrient deficiencies than the technology that is currently available. A cost-effective means to fortify a staple product of very high consumption can broaden the access of a population to fortified products and help reduce the burden and adverse impacts of micronutrient deficiencies.

Phase I activities will focus on the development of a fortification technology that is less costly than what is currently available, but still results in efficient and effective rice fortification with micronutrients at the appropriate levels to decrease micronutrient deficiencies. During Phase I it is expected that a technology prototype is developed for small rice mills that can effectively fortify rice with selected micronutrients.

Impact and Commercialization Potential: Many developing countries currently have some level of fortification of wheat flour. Machinery, therefore, is in place for wheat fortification. A rice fortification technology that can be integrated into existing technology would help expand the reach of fortification. Further, a cost-effective technology that can be used by small mills can also broaden the reach of fortified products. The expectation is that the proposed technology will meet market demand by manufacturers in countries willing to fortify rice, but who have been concerned about cost.

4. Mobile Application Development for Safer Medication Use in Pregnancy

Background: Women struggle with decisions regarding medication use in pregnancy due to concerns about potential risk to the fetus. Up to 9 out of 10 women report taking at least one medication sometime during pregnancy; however, for most medications, the safety or risk profile is either unknown or very difficult to find, making it difficult for healthcare providers and women to weigh the risks and benefits of different treatment options during pregnancy. This dilemma impacts two vulnerable patient populations --- pregnant women and their unborn children.

Pregnancy is experienced by 10% of US women each year, resulting in approximately 6 million pregnancies and 4 million births. Adverse fetal outcomes comprise a major public health burden in the United States, with birth defects affecting 1 in 33 births, preterm birth affecting more than 10% of all births, and approximately 26,000 fetal deaths occurring each year. Additionally, preterm birth and birth defects are the leading causes of infant mortality. Published research has shown an important potential for reducing adverse outcomes by shifting prescribing practices to medications with lower risk.

Both acute and chronic medical conditions that are relatively common in reproductive-aged women can require treatment with prescription or over-the-counter medication during pregnancy, such as infections, allergies, depression, asthma, thyroid disorders, diabetes, and migraines. Without treatment, the woman and/or her baby could be harmed. Pregnant patients may discontinue or underuse needed medications due to fear of potential fetal risk, whether this perception is founded or not.

A few existing databases provide an expert review and an evidence summary of the available literature on the fetal risks of specific medications during pregnancy, but these resources are not widely available to women or their healthcare providers and are thus underutilized. With no “gold standard” information source to consult regarding these health decisions, clinical uncertainty exists, leading to significant variation in clinical care, and thus vast potential to improve health equity and health outcomes for both mothers and their babies.

There is a searchable online database and corresponding mobile application for medication use while breastfeeding (LactMed, http://toxnet.nlm.nih.gov/help/lactmedapp.htm) that is available for iPhone/iPod Touch and Android devices. LactMed has recently been endorsed by the American Academy of Pediatrics’ Committee on Drugs, and could serve as an example for the requested application on safer medication use in pregnancy, including the need for endorsement by relevant professional societies to improve utilization and impact.

Specific Research Areas of Interest: The goal of this project is to design and develop a mobile application with evidence summaries for risks associated with specific prescription and over-the-counter medications used during pregnancy.

Impact and Commercialization Potential: This mobile app would help healthcare providers decide between clinical management options for the woman who wants to make the safest choice for protecting her developing (or future) baby while effectively managing her own health condition. The mobile application should be developed for multiple platforms (i.e., iPhone, Android), with one platform developed first as a prototype. The successful applicant should provide documentation that they have full access to one of the existing databases that provides an expert review and evidence summary of the available literature on the fetal risks of specific medications during pregnancy. The initial information will be available for search by specific medication (by both brand name and generic name), but the development should also include a future module for searching by maternal indication (e.g., depression) such that an evidence summary comparing the available treatment options can be presented. The application should be designed primarily for healthcare providers, but it should also be suitable for use by reproductive-aged women seeking this information.

For NCBDDD programmatic information, contact:

Brenda Colley Gilbert, Ph.D., MSPH
Director, Extramural Research Program Office
National Center for Chronic Disease Prevention and Health Promotion
Centers for Disease Control and Prevention
Mail Stop F-46
4770 Buford Highway, NE Atlanta, GA 30341
770-488-8390, Fax: 770-488-7863
Email: BColleyGilbert@cdc.gov

For grants specific, administrative information, contact:

Ms. Roslyn Curington
Grants Management Officer
Procurement and Grants Office (PGO)
Centers for Disease Control and Prevention
2920 Brandywine Road
MS E-09
Atlanta, GA 30341-4146
770-488-2832, Fax: 770-488-2777
Email: RCurington@cdc.gov

Ms. Tracey Sims
Grants Management Officer
Procurement and Grants Office (PGO)
Centers for Disease Control and Prevention
2920 Brandywine Road
MS E-09
Atlanta, GA 30341-4146
770-488-2739, Fax: 770-488-2777
Email: TraceySims@cdc.gov

NATIONAL CENTER FOR EMERGING AND ZOONOTIC INFECTIOUS DISEASES (NCEZID)

For additional information about NCEZID, please visit their web site at: http://www.cdc.gov/ncezid/about-ncezid.html

5. Multiplex, Quantitative Detection of Intestinal Multidrug-resistant Organisms (MDROs) and the Distribution of Major Taxa of the Microbiome

Background: Antibiotic resistance is a global public health challenge that has reached critical levels in healthcare settings where multidrug-resistant organisms (MDROs) threaten to segue clinical medicine into a post-antibiotic era. These MDROs include organisms such as vancomycin-resistant enterococcus (VRE), carbapenem-resistant Enterobacteriaceae (CRE), extended-spectrum beta-lactam resistant Enterobacteriaceae (ESBLs), and Clostridium difficile, all of which primarily colonize patients in the lower intestine where they undergo clonal expansion and often dominate the microbiome. A prerequisite for colonization by these intestinal MDROs is a disruption of the lower-intestinal microbiome that usually results from exposure to antibiotics, but may be contributed to by other medications, dietary changes, and diarrhea from viral and non-infectious causes. Following colonization, dominance of the lower intestinal microbiome by a particular MDRO (as defined by constituting >30% of the microbiome) is a risk factor for infection. Moreover, intestinal MDRO dominance, over and above low-level colonization, is associated with increased skin and environmental contamination and risk of transmission.

Specific Research Areas of Interest: The goal of this project is to develop a research grade diagnostic assay that simultaneously and quantitatively detects in stool, the presence and relative amounts of the previously described MDROs (i.e. CRE, VRE, ESBL, and C. difficile) along with major components of the microbiome described at higher taxonomic levels (e.g. phylum/class/order). It is anticipated this could be achieved by employing one of several currently available or a newly developed platform that allow performance of multiple, multiplex real-time PCRs with rarefaction curves, cross-standardized to allow combined analysis. However, other strategies and technologies could also be used to achieve the analytic objectives of: 1) detecting each MDRO with a known limit of detection that is relevant to commonly found levels of colonization (to the extent reported in the literature) in patients, 2) determining the abundance of MDROs relative to major taxonomic components of the lower intestinal microbiome

(e.g. degree of dominance), and 3) determining relative abundance of the major taxa of the lower intestinal microbiome to describe disruptions that may portend future near-term risk of MDRO colonization or infection (i.e. in patient found not to be already colonized).

Impact and Commercialization Potential: Investigations are underway to identify critical taxonomic and functional components of the intestinal microbiome that, when absent, confer risk for colonization or infection. Because these efforts are focused on the development of therapeutics and/or prophylaxis for MDRO (especially C. difficile) colonization or infection, these targets may not be well-suited for diagnosing the overall degree of microbiome disruption that predicts risk for these outcomes. In addition, both the DNA sequencing and bioinformatics resources required to generate and analyze either 16S ribosomal or deep DNA metagenomics data are likely to be beyond the reach of most clinical settings for a number of years. Meanwhile, current infection control and public health recommendations include active surveillance testing, at least under certain circumstances, to detect and contain transmission from patients who are asymptomatically colonized with the aforementioned MDROs, with C. difficile being a current exception.

6. Large-scale production of the CDC Autocidal Gravid Ovitrap for Control of Mosquito-Borne Diseases

Background: It has been recently estimated that globally there are 100 million dengue cases and 390 million dengue virus infections per year; making dengue the most common arboviral disease in the world. Dengue and its mosquito vectors are also re-emerging in subtropical and temperature zones in the US and Europe. At present, because there are no vaccines, vector control is the only available means to prevent and control dengue and other emerging arboviruses such as chikungunya and West Nile, and to some extent yellow fever, where a vaccine is available. A major limitation for controlling mosquito vectors is the lack of adequate tools for vector surveillance, so that control measures can be appropriately assessed. Furthermore, traditional vector control measures (insecticide spraying, elimination of containers producing mosquitoes) are not producing the expected results and these diseases continue to increase in incidence and geographic range. The CDC has developed the Autocidal Gravid Ovitrap (AGO) to capture the gravid female mosquito, which is the stage in the life of the mosquito most likely to transmit viruses. The AGO is an efficient, relatively inexpensive tool to monitor mosquito populations and should be able to solve the limitations of vector surveillance. The AGO lures gravid mosquito females by means of an olfactory attractant and the landing females get entangled in a sticky glue. In addition, the AGO has the potential to control dengue vector mosquitoes. Outbreaks of *Aedes aegypti*, the main dengue virus vector, have been suppressed by using 3 AGO traps per home in urban areas of Puerto Rico. Mosquito outbreak suppression has the potential to suppress dengue outbreaks.

Specific Research Areas of Interest: The goal of this project is to adapt the hand-made, AGO prototype for mass-production and its eventual commercialization, so that the trap becomes available to vector control programs and the public. This would include design and development of plastic injection mold(s) needed for mass-producing the trap. Currently, the trap is hand-made from components that can be purchased commercially. The AGO developed for mass-production must be compared to the present hand-made AGO to show that it is equivalent in resistance and durability to weather and field use, and has equivalent mosquito trapping efficiency.

Impact and Commercialization Potential: There is a need to make an affordable AGO that could be widely used by vector control programs and the public for both mosquito surveillance and control. Mass-produced traps need to be tested to determine if they keep the properties of the original design in terms of efficiency in capturing mosquitoes. Once this is accomplished, it is anticipated that studies will be conducted to determine if the AGO can actually suppress dengue outbreaks in urban settings.

For NCEZID programmatic information, contact:

Ms. Barbara Stewart

Deputy Director, Extramural Research Program Office
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Center for Disease Control and Prevention
1600 Clifton Road
Mail Stop E-60
Atlanta, Georgia 30333
404-718-8832; Fax: 404-718-8640
Email: BStewart@cdc.gov

For grants specific information, contact:

Ms. Anella Higgins
Centers for Disease Control and Prevention
Procurement and Grants Office
2920 Brandywine Road
MS E-15
Atlanta, GA 30341-4146
770-488-2710; Fax: 770-488-8350
Email: AHiggins@cdc.gov

National Center for H**IV**/A**IDS**, V**IRAL** H**EPATITIS**, STD, **AND** TB P**REVENTION**

For additional information about NCHHSTP, please visit their web site at: http://www.cdc.gov/nchhstp/

7. e-clinical STD guideline storage and dissemination

Background: The STD treatment guideline is the most widely recognized clinical guideline from CDC dating back to the 1980s. CDC is working with a number of Community Health Centers (CHCs) and Federally Qualified Health Centers (FQHCs) with established EMR systems to test the feasibility of converting some of the treatment guidelines into a computer ready format and make them available as clinical decision support modules in the future. This platform would provide a technical framework to house suitable STD treatment guidelines and their e-specifications. In 2008, CDC's Division of Viral Hepatitis published updated and expanded guidelines for testing for chronic Hepatitis B virus (HBV) infection and recommendations for public health evaluation and management for chronically infected persons and their contacts ("Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection"). Enhancing access to these guidelines will facilitate testing and management of persons at risk for HBV infection, including foreign-born person from high and medium HBV endemic countries. Currently, lack of recording patients' country of birth in medical records and limited provider knowledge of HBV prevalence in various countries are barriers to identifying at risk foreign born persons recommended for testing.

Specific Research Areas of Interest: The goal of this project is to create a cloud based, platform neutral, e-clinical STD/HBV guidelines storage database that will be able to connect with EMR systems and provide e-clinical guidelines ready to be inserted into EMR systems on demand. Using the STD/HBV clinical guidelines as a prototype for the electronic storage of clinical information and their ability to interact with clinical guidelines stored in compatible format will create the potential for computer-based tools to help clinicians significantly enhance the quality of medical care and increase the efficiency of medical practice. These tools may include reminder systems that identify patients who are due for preventative care interventions, alerting systems that detect contraindications among prescribed medications, and a physician ordering system that would present a prebaked orders menu to the physician, if needed at the point of care.

Impact and Commercialization Potential: Cloud-based architecture would enable the storage and distribution of these e-clinical guidelines to different software platforms and EMR vendors. Small

businesses could then extend this concept to store clinical guidelines to various professional bodies such as Infectious Disease Society of America (IDSA) and the American Medical Association (AMA) among others, and could also work with a number of federal agencies involved in e-measures and e-clinical guideline domain such as NIH, AHRQ and the ONC, HHS (Office of the National Coordinator for Health Information Technology).

8. Application for Improving Point of Care testing in Early Stage Syphilis Diagnostics

Background: Syphilis remains an important public health problem particularly in low income settings and in resource poor health care systems. Syphilis infection has been associated with higher risk for HIV infection and congenital infections remain an area of unmet diagnostic need. Mother to child transmission (MTCT) can be fully controlled with proper diagnostic tools and accessibility for point of care testing of pregnant women. A cost effective and simple diagnostic tool could be applied to reach low income and remote populations to prevent potential MTCT of syphilis.

Specific Research Areas of Interest: The goals for this project are to develop reliable, sensitive and specific assays for rapid use in a clinical setting using serological or proteomic detection of infection for syphilis. The proposed application will promote the use of diagnostic testing through development of a simple and cost effective device for rapid point of care patient testing that will impact patient care in real time. Utility in preventing patient loss to follow up requires a rapid test with high sensitivity and specificity that requires little technology for completion. The application should address test development in the context of cost, ease of use, accuracy and utility in preventing patient loss to follow up. Early phase activities are expected to provide a pilot model of detection system specific for Syphilis using either Treponemal antigen, Reagin (RPR) or both analytes as describe in the traditional Syphilis algorithm.

Impact and Commercialization Potential: The improvement of point of care testing in early stage Syphilis has the potential to fuel novel design and drive innovation towards rapid test platforms and utility for early detection and accuracy.

For NCHHSTP programmatic information, contact:

Ms. Barbara Stewart
Deputy Director, Extramural Research Program Office
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Center for Disease Control and Prevention
1600 Clifton Road
Mail Stop E-60
Atlanta, Georgia 30333
404-718-8832; Fax: 404-718-8640
Email: BStewart@cdc.gov

For grants specific information, contact:

Ms. Edna Green
Centers for Disease Control and Prevention
Procurement and Grants Office
2920 Brandywine Road
MS E-15
Atlanta, GA 30341-4146
770-488-2858; Fax: 770-488-2828
Email: EGreen@cdc.gov

NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

For additional information about NCIPC, please visit their web site at: http://www.cdc.gov/injury/index.html. Only applications that address the topics below will be considered for funding by NCIPC.

9. Innovations in Electronic Health Record (EHR) Systems in Primary Care to Reduce Older Adult Falls

Background: Falls and their associated injuries are a growing public health concern—responsible for over 20,000 deaths and 2.3 million emergency department visits nationwide, and costing over $30 billion annually. The U.S. population is aging. People aged 85 and older are the fastest growing segment of the elderly population as well as those with the highest risk of falls and fall injuries. On an individual basis, healthcare providers can prevent falls through clinical falls risk assessment, treatment and referral. Yet, primary care providers report that they do not know how to assess fall risk or do not have adequate knowledge about fall prevention. To address this need, CDC has developed a comprehensive fall prevention toolkit for healthcare providers, STEADI, based on the American Geriatrics Society (AGS) practice guideline to promote falls risk assessment and management (http://www.cdc.gov/homeandrecreationalsafety/Falls/steadi/index.html). Innovations in Electronic Health Record (EHR) systems significantly could increase adoption of the STEADI tool kit and clinical practice guideline more broadly. Computerized clinical decision support systems that lead physicians through practice guidelines and tools, like STEADI, and facilitate use of quality metrics within EHRs, can help providers improve clinical care while increasing efficiency, improving patients' health outcomes, reducing fall-related injuries and hospitalizations, and lowering health care costs.

Specific Research Areas of Interest: The goals of this project include developing innovative EHR technology that will facilitate healthcare providers' use of fall risk assessment procedures, treatment, and referrals within the primary care practice setting and simultaneously streamline health care reimbursement procedures. Another goal of this project is the development of a module on the STEADI toolkit that could be embedded within existing EHR systems to help with clinical decision support and a reimbursement module. For example, physician practices participating in CMS' Physician Quality Reporting System (PQRS) can document fall risk assessment using the following two codes: Falls Risk Assessment (CPT-II Code 3288F) [PQRS #154] and Falls: Plan of Care (CPT-II Code 0518F) [PQRS #155]. In addition, objectives for Stage 2 Meaningful Use will include a 2014 clinical quality measure (CQM) for eligible health professionals (EPs): Percentage of patients $\geq$ 65 years screened for future fall risk.

Impact and Commercialization Potential: Innovations in EHR technology might include coding for CQMs linking to clinical decision support tools, such as alerts and reminders, which will facilitate using specific screening assessments and referral options. Such technology enhancements would call special attention to older adults' falls risk, encourage using clinical quality metrics, and potentially facilitate billing.

10. Developing a Fall Detection System for Older Adults

Background: Among older adults, falls and their associated injuries are a growing public health concern—responsible for over 20,000 deaths and 2.3 million emergency department visits nationwide, and costing over $30 billion annually. Older adults who fall often restrict their activities and social contacts, which can impair their quality of life. Technological systems have been developed to broadcast an alert when an older adult falls – discriminating between a fall event and the normal activities of living. Systems can use environmental sensors (e.g., cameras, floor sensors) and/or wearable devices (e.g., accelerometers with electronic sensors on clothing). Using such systems can increase older adults' confidence and independence.

Specific Research Areas of Interest: The goals of this project include developing or enhancing innovative assistive technology that can facilitate detecting older adult falls. Developers must include

older adults in the development process and also include procedures for protecting older adults' privacy. The technology should be amenable to testing with older adults in realistic settings and for extended time periods to evaluate real-world applicability. Consideration must be paid to reducing the number of false alarms as well as inappropriate alerts, so as to increase the likelihood of adoption in geriatric practice (e.g., by encouraging patient use).

Impact and Commercialization Potential: The technology should advance previous applications by integrating the technology into devices used routinely (e.g., smartphones), enhancing the fall detection algorithm, or facilitating integration with electronic health records (e.g., communicate fall events to the health provider through the electronic medical record system). There are opportunities to advance technologies by integrating sensors into commonly used devices such as smartphones, and by enhancing detection algorithms. Such refinements could increase the performance, usability, and acceptance of these devices, as well as provide better real-time data about fall events.

11. Innovations to Reduce Traffic Deaths and Injuries

Background: Traffic crashes account for half of all unintentional injury deaths, are the leading cause of death for people ages 5–34 in the United States, and result in nearly 5 million serious injuries. In one year, the cost of medical care and productivity losses associated with traffic injuries in the United States exceeded $99 billion. Globally, road traffic injuries kill 3,000 persons daily. The risk of motor vehicle crashes is highest among teen drivers age 16- to 19-year-olds. Alcohol is a contributing factor in 31% of motor vehicle crash fatalities, and I in 4 of the alcohol-impaired drivers in these crashes have had their driver license suspended or revoked in the previous 3 years. In 63% of fatal crashes, the occupant killed was not wearing a seat belt. Excessive speed has been identified as a key risk factor in traffic injuries, influencing both the risk of a crash and the severity of the injuries that result. Motor vehicle crashes result from a combination of environmental, human behavioral and vehicle-related factors. Modifying any or all can substantially alter the risks of a crash, and the chances of survival. Modifying any one factor can influence all others, and feedback loops about the performance of the vehicle, road and environment, and driver fitness can reduce risks and errors, but this requires adaptive technology. Currently, there are limited accessible means for warning drivers of impending dangers such as perceptual deficits, driver error, hazardous road conditions and environments, and suboptimal vehicle performance that may influence crash risks. Drivers need such tools to make life-saving decisions easier and more automatic.

Specific Research areas of interest: CDC is particularly interested in the development of improved environmental, engineering, and human factor controls (including retrofit vehicle solutions) with the potential to reduce motor vehicle crashes and the injuries that result. Projects might include the development of real-time technologies such as "cues to safe action" while driving based on driver fitness, vehicle performance characteristics, environmental conditions, and road -based information. Technologies might also include sensors that detect alcohol, or driving motions and activity of individuals with license sanctions and restrictions. Technology that can be applied in both occupational driving and private vehicle use in domestic rural settings is of high interest, along with applications of this technology to assist persons with cognitive or psychomotor limitations (e.g., persons who become distracted while driving, drowsy driving and fatigue, alcohol impaired or drug impaired driving, and age-related changes). Innovations that would be suitable for overseas applications in low and middle-income countries are highly desirable.

Impact and Commercialization Potential: Innovative technologies that can assist in modifying drivers' risk behavior, such as alcohol-impaired driving, are still evolving and ripe for exploration (e.g., alcohol detection systems, license sanction enforcement systems). These innovations would be marketable to parents, law enforcement, insurance companies, and others.

12. Innovations to Reduce Residential Fire Deaths and Injuries

Background: Deaths from fires and burns are the third leading cause of fatal home injury. On average in the United States in 2010, someone died in a fire every 169 minutes with 85% of these deaths occurring in homes. In 2010, fire departments responded to 384,000 home fires in the United States, which claimed the lives of 2,640 people (not including firefighters) and injured another 13,350. Cooking is the primary cause of residential fires; however, smoking is the leading cause of fire-related deaths. Most victims of fires die from smoke or toxic gases and not from burns. Certain people are more at risk for injuries and death including children under 5 years and adults over 65 years. Fire-related injuries are expensive with one year of fatal and nonfatal fire/burn injuries totaling $1.3 billion in medical costs alone. Smoke alarms are an important device to alert residents to fire danger. No smoke alarms were present in more than one-third (38%) of the home fire deaths. However, functionality is also important; in one-quarter (24%) of the home fire deaths, smoke alarms were present but did not sound, many due to missing, disconnected or dead batteries. More than one of every three (36%) fatal fire victims never wakes up before being injured. Even functioning smoke alarms may not awaken young children or older adults. These groups may have difficulty hearing the alarm, alerting or responding to it, or exiting the house.

Specific Research Areas of Interest: CDC is interested in the development and improvement of technologies for fire prevention, alerting of residential fires, and fire suppression. Projects might include the development or improvement of monitoring/alerting systems with the potential to reduce residential fire occurrences, injuries and deaths. Currently there are limited inexpensive options for reliably alerting children or other at risk groups of the presence of a fire. There is also room for innovation in products that prevent or suppress residential fires, such as sprinkler systems. Although the number of fatalities and injuries caused by residential fires has declined gradually over the past several decades, many residential fire-related deaths remain preventable and continue to pose a significant public health problem.

Technologies might include sensors that detect hazards or dangerous behaviors. Technology that aids persons with cognitive or psychomotor limitations (e.g., children, older adults, disabled persons, impaired persons) is of particular interest. For example, research might investigate what will reliably arouse children or older adults. Technologies that extend, improve, or simplify functionality of alerting systems at competitive prices are also desirable. Developments might include enhanced consumer products to improve outcomes (e.g., improved alerting), prevention of fire (e.g., heating systems, cooking systems), or developments that reduce spread or severity of fires (e.g., improved fire suppression systems, such as sprinkler systems).

For NCIPC programmatic information, contact:

Dr. Paul Smutz
Extramural Research Program Office
NCIPC, NCEH/ATSDR
Centers for Disease Control and Prevention
Mail Stop F-63
4770 Buford Highway, N.E.
Atlanta, Georgia 30341
770-488-4850, Fax: 770-488-1665
Email: WSmutz@cdc.gov

For grants specific, administrative information, contact:

Mr. Ralph Robinson
Centers for Disease Control and Prevention
Procurement and Grants Office
Mail Stop K-69
2920 Brandywine Road

Atlanta, Georgia 30341
770-488-2441, Fax: 770-488-2847
Email: RRobinson6@cdc.gov

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)

For additional information about NIOSH, please visit their web site at: http://www.cdc.gov/niosh/programs.

HIGH RISK INDUSTRIAL SECTORS IN NIOSH

Exposure assessment, engineering controls, and personal protective technologies (PPT) are needed to manage exposures to occupational hazards in high risk industrial sectors. These include manufacturing, services, mining, agriculture and construction sectors. Workers in the manufacturing sector, comprising an estimated 14 million paid workers in 2005, face risks that include machinery, repetitive motion, over-exertion, chemicals, nanomaterials, noise and shift work. In the services sector, work environments vary widely and these varied, and often uncontrolled, environments may put the estimated more than 65 million workers at risk of workplace injury, illness and death. The mining sector, comprised of over 300,000 paid workers in 2005 (not counting those in the oil and gas extraction sub-sector), face risks that include noise-induced hearing loss, falling materials, explosions, fires, powered haulage, overexertion, electrical equipment, and exposure to particulates and dusts including diesel emissions, coal dust and silica dust. 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. Each day, construction workers face injury hazards from falls, machines, electricity, motor vehicles, and other equipment and circumstances. Health hazards posed by construction work can include dusts, fumes, noise, and chemicals. Research is needed to develop control strategies, PPT, exposure assessment methods and interventions to reduce motor vehicle injuries and deaths in all these high risk industrial sectors.

The following research areas are of particular interest to NIOSH:

13. Control Technology and Personal Protective Equipment for High Risk Occupations

Background: Personal protective equipment (PPE) protects workers from death and disabling injuries and illnesses as well as from the specific threats of exposures to certain airborne biological particles, chemical agents, nanomaterials, splashes, noise exposures, fall hazards, head hazards, and fires. It is estimated that 20 million workers use PPE on a regular basis to protect them from job hazards and a total of 135,000 workers potentially could benefit from the use of PPE (Worker Health Chartbook 2004). 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. Research is needed to develop and evaluate control strategies and personal protective equipment for specific hazards and to assure their practicality and usability in workplaces in all the high risk industrial sectors.

For additional information about NIOSH PPE and Engineering control programs, please visit their web site at: http://www.cdc.gov/niosh/programs/ppt/ and http://www.cdc.gov/niosh/programs/eng/.

Examples of specific research areas of interest include, but are not limited to:

Conduct research on the ability of existing containment and control strategies to prevent releases and potential human exposures to engineered nanomaterials.

Conduct research to evaluate the effectiveness of personal protective equipment (PPE) in protecting workers against exposure to engineered nanomaterials. Provide data to fill knowledge gaps and support guidance for the selection and use of gloves and protective garments to prevent exposures. Respiratory protection research needs to be extended to a broad range of engineered nanomaterials.

Develop a heads-up display coupled with a personal noise exposure monitoring system. Personal noise alert “badges” and personal noise dosimeters exist, but do not have an effective way to alert the user immediately when a noise hazard occurs. A system that displays a warning within the user’s visual field (via lights on protective eyewear, hardhat, etc.) would facilitate hazard recognition.

Develop an inexpensive hand-held earplug test device based on the NIOSH QuickFit concept. Studies of hearing protector users have shown repeatedly that average protection values are much lower than the labeled Noise Reduction Ratings (NRR) determined in laboratories. A QuickFit test system would help workers determine if their hearing protection is giving them at least 15 decibels of attenuation.

Develop innovative engineering control approaches and technologies for reducing asphalt exposures in roofing, and skin exposures and disease in construction workers.

Conduct research to understand PPE integration and interoperability issues. In most cases, individual PPE are currently used without consideration for their ability to function together. Research is needed to test interfaces among different PPT and components. Current interfaces do not provide seamless integration of PPT components resulting in reduced comfort, fit, usability, and protection for the wearer as well as logistical challenges for safety managers and employers.

Develop innovative educational and professional training materials suitable for today’s diverse workplace on the role of PPT in occupational safety and health. This is especially critical for high risk occupations. Innovative methodologies including social media should be explored and evaluated to demonstrate their effectiveness at improving workplace safety and health. For example, to what extent can mobile application media be focused on worker safety and health to provide up-to-date PPT information to a diverse range of employers and employees’ through portable communication devices?

Impact and Commercialization Potential: The impact of the proposed research will prevent work-related injury, illness, and death by advancing the state of knowledge and application of personal protective technologies (PPT). Potential products include technical methods, processes, techniques, tools, and materials that support the development and use of personal protective equipment worn by individuals to reduce the effects of their exposure to a hazard. NIOSH will continue its collaborative efforts in partnership with labor, industry, government, and other stakeholders.

14. Exposure Assessment Methods for High Risk Occupations

Background: Exposure assessment provides multi-disciplinary strategies and methods to anticipate, recognize, evaluate, control, and confirm effective management of occupational health stressors, exposures to those stressors, and resulting health risks. Major gaps in current approaches include: (1) the lack of practical methods for hazard identification and measurement that can be applied at reasonable cost in many workplaces where health stressors may exist, (2) the lack of validated, noninvasive biological methods for monitoring relevant exposure and resulting dose, and (3) the lack of strategies and methods for epidemiologic studies to demonstrate either a dose-response effect or a conclusion of no association between the agent and disease in the complex environments of today's workplaces.

For additional information about NIOSH Exposure Assessment programs, please visit their web site at: http://www.cdc.gov/niosh/programs/expa/.

Examples of specific research areas of interest include, but are not limited to:

As the rapidly emerging new approach to material science, two areas of research are needed to support effective assessment of worker exposure to engineered nanomaterials. 1. Real-time sensors capable of reliably detecting nanoparticles and providing information on size distribution and count, and that can be used for personal monitoring; and 2. Development of methods that can detect and quantify the presence of engineered nanomaterials in samples collected for the purpose of characterizing exposures. These methods need to be cost-effective and available to the OS&H practitioner community. Broader application to general public health assessments should be factored into the research.

Develop new or improved methods to measure occupational health stressors such as psychological and ergonomic factors, noise, chemicals, particles and fibers, physical agents, non-ionizing radiation, or mixtures of stressors in the work environment. Enhanced measurement performance and functionality can include sensitivity, selectivity, size and weight considerations, ease of use, and capabilities to measure multiple analytes simultaneously.

Develop or adapt easy-to-use, direct-reading instruments and test kits to rapidly and inexpensively measure exposures in a variety of workplaces. Critical applications include routine monitoring, evaluating the success of control technologies, and supporting epidemiological studies. For example develop a sound level meter to monitor worker noise exposure that can be used in underground coal mines.

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, work tasks and workers can be categorized according to hazard bands and exposure bands, and at-risk workers can be identified and protected.

Develop a computerized system that can be used to predict worker noise exposure from mining machine noise emissions. The system would include an acoustic model of mining environments and algorithms to characterize exposure based on noise source characteristics. The main application for this technology would be for mining machine manufacturers to evaluate the potential effects noise controls during the design process. If the impact of design changes on exposure reduction can be accurately predicted without the need for extensive field measurements, innovative noise controls can reach implementation much more quickly.

Impact and Commercialization Potential: This research will lead to the development of practical solutions and prevention activities to address complex problems that cause occupational diseases, injuries, and fatalities and that will lead to reductions in occupational injuries and illnesses among all workers. NIOSH is committed to building and maintaining collaborative partnerships with international organizations in labor, industry, and government, as well as with other interested stakeholders. Research to Practice (r2p): This research will lead to the development and translation of exposure assessment methods and research findings into prevention practices and products that will be adopted in occupational settings.

15. Work-related Injuries from Motor Vehicle Crashes

Background: The risk of injury associated with on-the-job operation of motor vehicles affects millions of U.S. workers. Motor vehicle-related incidents are consistently the leading cause of work-related fatalities in the United States. Of over 43,000 work-related fatalities reported by the Bureau of Labor Statistics

between 2003 and 2010, 15,396 (36%) were associated with motor vehicles. The public health toll for 2003-2010 included:

10,202 deaths in single- or multiple-vehicle crashes on public roadways
2,487 deaths in crashes that occurred off the highway or on industrial premises
2,707 pedestrian worker deaths as a result of being struck by a motor vehicle

Over the same period, workers incurred nearly 400,000 lost-workday injuries due to these incidents. Crash-related fatalities and serious injuries have a devastating impact on workers and their families, and on the economic health and productivity of American businesses. In some instances, e.g., the operation of heavy trucks, work vehicles also have an impact of the safety of the motoring public.

The virtual NIOSH Center for Motor Vehicle Safety coordinates the CDC/NIOSH response to this pressing worker safety issue. Many NIOSH programs include motor vehicle crashes among their top injury prevention priorities: Traumatic Injury; Transportation, Warehousing, and Utilities; Wholesale and Retail Trade; Oil and Gas Extraction; Public Safety; and Global Collaborations.

Examples of specific research areas of interest include, but are not limited to:

The highest priority is to develop, implement, and evaluate interventions in an effort to build the scientific evidence base to guide prevention of work-related motor vehicle crashes and resulting injuries. This may be achieved by developing new design concepts and standards for use by national standard-setting organizations in updating or developing design standards for specialized work vehicles, enhancing effective interventions for driver training and assessment to reduce work-related motor vehicle crashes, evaluating the effectiveness of technology- or management-based intervention strategies to reduce the incidence or severity of work-related motor vehicle crashes, and enhancing engineering controls for preventing work-related crashes and injuries.

Impact and Commercialization Potential: Application of evidence-based interventions is expected to have a large impact on reducing the incidence and severity of work-related motor vehicle crashes. This will yield substantial public health benefits, and will positively affect workers' compensation and health insurance premiums and costs. CDC/NIOSH has well-established working relationships with employers, their trade associations, and standards-setting organizations, and is therefore strongly positioned to communicate findings and guidance to potential users. CDC/NIOSH also has strong infrastructure to facilitate the transfer of technology-based interventions to the marketplace. Given the extremely short induction period between exposure and injury occurrence, CDC can make a measurable difference in a very short period of time (< 4 years).

Visit the NIOSH homepage for more information on NIOSH's research program areas http://www.cdc.gov/niosh/homepage.html.

For NIOSH programmatic information, contact:

Steve Dearwent, Ph.D., M.P.H.
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
Mail Stop E74
1600 Clifton Road, N.E.
Atlanta, Georgia 30333
404-498-6382, Fax: 404-498-0751
Email: SDearwent@cdc.gov

For grants specific, administrative information, contact:

Ms. Mary Pat Shanahan
Centers for Disease Control and Prevention
Procurement and Grants Office, Field Branch V
PO Box 18070
626 Cochrans Mill Road
Pittsburgh, PA 15236-0070
412-386-4453, Fax: 412-386-6429
Email: MShanahan@cdc.gov

FOOD AND DRUG ADMINISTRATION (FDA)

FDA will accept SBIR grant applications on the April 5, August 5, and December 5, 2014 submission dates.

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get accurate, science-based information they need to use medicines and foods to improve their health.

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, post marketing 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, post marketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., data mining 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 practitioners 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 FDA is responsible for the safety of the vast range of food Americans eat; about 80 percent of all food sold in the United States. This includes everything except for the meat, poultry, and processed egg products that are regulated by the USDA. Consequently CFSAN seeks research designed to complement and accelerate efforts aimed at the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics. CFSAN conducts research, and develops regulations, guidance and standards related to the composition, quality, nutrition, and safety of food, food additives, colors, and cosmetics. The Center 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 and food additives.

CFSAN maintains an active research program that is focused on the following priorities; ensuring the safety of food, dietary supplements and cosmetics; improving nutrition; and promoting the security and integrity of the food supply. The Center's research activities are intended to; support the FDA's regulatory activities; reduce the incidence of foodborne illness by improving our ability to detect and quantify foodborne pathogens, toxins, and chemicals that could jeopardize the safety and security of the food supply; find new and improved ways to control these agents; and safely produce, process, and handle food and food products. FDA is committed to reducing the incidence of foodborne illness to the greatest extent feasible while at the same time protecting the nation's food supply. Mission-critical knowledge gaps are addressed through translation research focused on the risks associated with FDA regulated products throughout their life cycles, from production to consumption. Ideally extramural research is sought that complements the Center's intramural research efforts, and which will enhance the Agency's and the

Nation's ability to reduce the incidence of foodborne illness and protect the integrity of the nation's food supply. FDA's mission-critical needs require that the research not simply end with the generation of new knowledge and technologies, but extend to the validation of new approaches by using realistic conditions that accurately reflect the diversity of the food industry and offer potential solutions that can be accept by 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 effectiveness standards and good manufacturing practices regulations, operates post market 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 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.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Examine the setup, documentation and optimization of our Sun Grid Engine (SGE). The architecture of this networking application is particularly suited to managing surge capacity in high performance computing. The modeling of many physiologic functions and bioinformatic analyses can take months or even years to run on a standard desktop computer. The SGE takes the overall problem and distributes it to a cloud of computers on a network so that no user knows, or cares, if a computation is performing in the background on their machine. As FDA rolls out laptops with multi-core CPU's and which are equipped with prodigious amounts memory this experiment in "cloud computing" could become a reality on the Whiteoak Campus. The scope of work would be to develop, document, and provide training systems for developers, network architects, and users on working methodologies for the integration of cloud computing with the existing FISMA compliant conventional networking.

B. Develop a high-speed, low light spectral CMOS linear imaging system to measure complete spectra of multiple variables from living tissue. Complete spectra of fluorescence signals (including auto-fluorescence and FRET) could be measured along a line at high speeds (10 kHz) with a rectangular CMOS grid (e.g. 10 x 1,000 pixels -> 10 sites 1000 wavelengths).

C. Develop bioassays/biosensors to identify injurious levels of nerve stimulation utilizing bioluminescence and neurotransmitter detection technologies. Research capabilities needed include voltage clamp, current clamp and extracellular techniques in peripheral nerves and brain slices to explore stimulation protocols that release neuroactive substances released in injury and inflammation which are not normally evoked under normal physiological conditions.

D. Design, build, and validate a phantom that is traceable to a national metrology institute (NMI) such as NIST (or any other NMI) to improve the accuracy and clinical utility of bone mineral density measurements made using dual energy X-ray absorptiometry (DXA). The calibration phantom should be constructed using biosurrogate materials with known/tabulated data for body tissue and tissue substitutes.

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.

Research and development opportunities within the Center for Veterinary Medicine that lend themselves to performance by small businesses include, but are not limited to, the following areas of interest:

A. Development, for the specific purpose of obtaining approval or conditional approval, of products for the treatment, control or prevention of diseases or conditions occurring in minor species or small numbers of major species.

B. Development and validation of high throughput/screening quantitative and qualitative analytical methods for analyzing drugs, additives, and contaminants in animal tissues and feeds.

C. Development of methods to determine absorption, distribution, metabolism, and excretion of drugs, feed additives and contaminants (microbial and chemical) in food animals, including minor species.

D. Development of new biomarkers and models for determining the safety and effectiveness of veterinary drugs and food additives in domestic animals, including minor species.

E. Development of methods to determine the effects of drugs, food additives, and contaminants (microbial and chemical) on immunological and physiological functions of domestic animals, including minor species.

OFFICE OF CRITICAL PATH PROGRAMS

The Office of Critical Path Programs, in FDA's Office of the Chief Scientist, coordinates the cross-agency Critical Path Initiative (CPI), FDA's strategy for transforming the way medical products are developed, evaluated, and manufactured. CPI activities are under way throughout the Agency, from the product centers to the Office of the Commissioner. For details, see http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/default.htm. Collaboration is key to the CPI initiative because bringing safe, effective, and innovative therapies to the American public requires FDA to leverage the resources and expertise of all stakeholders, including other Federal agencies, academia, healthcare professionals, patient and consumer groups, regulated industry, and health-related organizations. In 2008, CPI collaborations involved 84 government agencies, universities, industry leaders, and patient groups from 28 states and 5 countries on a raft of groundbreaking research projects.

Research and development opportunities within FDA that lend themselves to performance by grantees include, but are not limited to, the following:

A. Studying the immunological correlates of TB immunity and developing tools to evaluate TB vaccine efficacy.

B. Developing study models for testing combination-antimicrobials as a strategy to prevent the development of drug resistance.

C. Developing new approaches to preclinical safety testing.

D. Identifying biomarkers for safety and efficacy evaluation of medical products.

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 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.

B. 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.

C. 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

For additional information on research topics and administrative and business information, contact:

Ms. Kimberly Pendleton Chew
Chief, Grants Management Officer
301-827-9363, Fax: 301-827-0505
Email: kimberly.pendleton@fda.hhs.gov

or

Mr. Martin Bernard
Grants Management Specialist
Grants and Assistance Agreements Team
301-443-5869, Fax: 301-827-0505
Email: Martin.Bernard@fda.hhs.gov

Food and Drug Administration
Division of Acquisition Support and Grants
5630 Fishers Lane - HFA 500
Rockville, MD 20857

ADMINISTRATION FOR CHILDREN AND FAMILIES

The Administration for Children and Families (ACF), within the Department of Health and Human Services (HHS) is responsible for federal programs that promote the economic and social well-being of families, children, individuals, and communities. ACF partners with State and local governments, for-profit and non-profit organizations, faith- and community-based organizations, American Indian Tribes and Native American communities to design, administer and promote programs in areas such as child welfare, childcare, Head Start, healthy marriage, Temporary Assistance for Needy Families (TANF), and responsible fatherhood.

The Office of Planning, Research and Evaluation (OPRE) facilitates ACF's SBIR investments. The Office provides guidance, analysis, technical assistance, and oversight to ACF programs on strategic planning aimed at measurable results; research and evaluation methodologies; demonstration testing and model development; statistical, policy and program analysis; synthesis and dissemination of research and demonstration findings.

The focus of the research topics for SBIR should reflect the research and programmatic interests of ACF. Particular areas of interest for ACF include but are not limited to:

- Adoption and Foster Care
- Child Abuse & Neglect
- Child Care
- Child Support
- Developmental Disabilities
- Early Head Start
- Energy Assistance
- Family/Domestic Violence
- Fatherhood and Healthy Marriage
- Head Start
- Native American and Tribal Programs
- Refugee Resettlement
- Human Trafficking
- Temporary Assistance for Needy Families
- Youth Development

For additional information on ACF programs and research, please visit the ACF web site at http://www.acf.hhs.gov and the Office of Planning, Research and Evaluation's web site at http://www.acf.hhs.gov/programs/opre/index.html.

For additional information on research topics, contact:

Anne F. Bergan
Social Science Research Analyst
Office of Planning, Research and Evaluation
Administration for Children and Families
370 L'Enfant Promenade, SW
Washington, DC 20447
202-260-8515, Fax: 202-205-3598
Email: abergan@acf.hhs.gov

For administrative and business management questions, contact:

Edeltraud Fernandez
Budget Officer/Staff Assistant
Office of Planning, Research and Evaluation
Administration for Children and Families
370 L'Enfant Promenade, SW
Washington, DC 20447
202-401-2346, Fax: 202-205-3598
Email: efernandez@acf.hhs.gov

APPENDIX A: NATIONAL INSTITUTES OF HEALTH SBA-APPROVED SBIR/STTR TOPICS FOR AWARDS OVER STATUTORY BUDGET LIMITATIONS

National Institutes of Health SBA-Approved SBIR/STTR Topics for Awards over Statutory Budget Limitations

1/1/2014

NIH has received approval from SBA for the topics listed within for budgets greater than $225,000 for Phase I SBIR/STTR awards and greater than $1,500,000 for Phase II SBIR/STTR awards for the PHS 2014-2 SBIR and STTR Omnibus grant solicitations. Applicants are **strongly encouraged** to contact NIH program officials prior to submitting any award budget in excess of these amounts. Applicants are also required to follow NIH Institute- and Center-specific budget guidance found in PHS 2014-2 SBIR/STTR Program Descriptions and Research Topics for NIH, CDC, FDA and ACF.

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NATIONAL CANCER INSTITUTE (NCI)

A. Therapeutics (e.g. Small Molecules, Biologics, Radiomodulators, and Cell-based Therapies)
B. In Vitro and In Vivo Diagnostics (e.g. Companion Diagnostics and Prognostic Technologies)
C. Imaging Technologies (e.g. Agents, Devices, and Image-Guided Interventions)
D. Devices for Cancer Therapy (e.g. Interventional Devices, Surgical, Radiation and Ablative Therapies)
E. Agents for Cancer Prevention (but not “Technologies for Cancer Prevention”)
F. Development of Low Cost Technologies for Global Health
G. Development of Companion Diagnostics
H. Vaccine Development for Cancer Prevention
I. Novel Technologies to Address “Undruggable” Drug Targets

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS)

A. Innovative platforms for identification and prioritization of targets for therapeutic intervention with clear clinical impact

B. Technologies to determine alternative uses for existing therapeutic interventions

C. Tools and technologies to allow assaying of activities of compounds on currently “non-druggable” targets

D. Phenotypic assay development, including stem cell technology platforms for human “disease in a dish” applications and the evaluation of toxicity

E. Co-crystallization high-throughput screening techniques

F. Small molecule and biologics analytical characterization

G. Tools and technologies that increase the predictivity or efficiency of medicinal chemistry, biologic, or other intervention optimization

H. Accelerate bioengineering approaches to the development and clinical application of biomedical materials, devices, therapeutics, and/or diagnostics

I. Tools and technologies that increase the efficiency of human subjects research, including development of technologies that facilitate rapid diagnosis and/or clinical trial recruitment and subject tracking, IRB evaluation, and/or regulatory processes

J. Novel platforms, technologies and tools to enable clinical and translational research, particularly those with mechanisms for inclusion of patient reported data

K. Searchable access to information about researchers and their expertise, including but not limited to their publications, published data sets, methods, patents, clinical trials, partnerships, collaborators, and clinical specialty/expertise (if applicable)

L. Tools for meaningful sharing of research data with low barrier for provision and user friendly access

M. Searchable access to information about research resources, facilities, methods, cells, genetic tests, molecules, biologic reagents, animals, assays, technologies with links to their use in published research studies

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)

A. Biomarkers which correlate with efficacy of CAM therapies

B. Standardized, reliable and economical tools that correlate with brain imaging in response to CAM treatment;

C. Technical imaging tools or instruments for studying manual therapies

NATIONAL EYE INSTITUTE (NEI)

Retinal Diseases

A. New therapeutic approaches for inflammatory and degenerative diseases and for inhibition of abnormal angiogenesis in the retina and choroid

Corneal Diseases

A. Therapeutic agents and drug delivery methods for the treatment of corneal injury, infection, dry eye, ocular pain, and other ocular surface disorders

Glaucoma and Optic Neuropathies

A. New therapeutic agents for treatment of glaucoma

Visual Impairment and Blindness

A. New or improved devices, systems, or programs that meet the rehabilitative and everyday living needs of blind or visually-impaired persons

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

A. Biomedical technologies (medical devices, instruments, pharmaceuticals, drugs, therapeutics, vaccines, diagnostics and biologics) for heart, lung, blood, and sleep related diseases and disorders requiring Federal regulatory approval (FDA) or clearance to be commercialized.

B. Small and large animal testing of products of tissue engineering and regenerative medicine, drugs, medical devices, therapeutics, and biologics and studies involving *in vivo* animal experiments for heart, lung, blood, and sleep related diseases and disorders.

C. Clinical trials and other experiments involving human subjects for heart, lung, blood, and sleep related diseases and disorders.

D. Therapeutics (drugs, devices, or biologics) development for heart, lung, blood, and sleep related diseases and disorders.

E. Device development for heart, lung, blood, and sleep related diseases and disorders

F. Diagnostics development for heart, lung, blood, and sleep related diseases and disorders.

G. Investigation of biomarkers and biosignatures of heart, lung, blood, and sleep related diseases and disorders.

H. Technologies to enhance clinical research for heart, lung, blood, and sleep related diseases and disorders.

I. Advanced instrumentation and high throughput tools for biomedical research in heart, lung, blood, and sleep related diseases and disorders.

J. Tools and platforms to improve the dissemination and implementation of evidence-based interventions for heart, lung, blood, and sleep related diseases and disorders.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

A. Development of novel or significant improvements on current next generation sequencing technology

B. Bioinformatics software for genomic, genetic and sequence data analysis, functional genomics and genomic data integration

C. Genomics tools ranging from new instruments to sophisticated molecular biology kits

D. Incorporating genomic results into electronic medical records

E. Informatics tools that assist in delivering genomic medicine to patients

F. Single cell genomic analysis

NATIONAL INSTITUTE ON AGING (NIA)

Division of Behavioral and Social Science (DBSR)

M. Development and translation of behavioral economics approaches (incentives or disincentives) to motivate sustainable behavior change to improve health and well-being.

4. Increasing levels of physical activity or promoting treatment adherence
5. Addressing biases such as loss aversion, errors in affective forecasting, present bias, ambiguity effect, base-rate neglect, and susceptibility to framing effects in health and financial decision making
6. Using information, or the mode of data presentation to systematically improve decision making (e.g., through “nudges,” policies, or practices that constrain choices)

N. Development of robotics applications to aid elderly

3. Socially assistive robots allowing elderly to remain independent in their homes. Technology could support machine cognition, language understanding and production, human-robot interaction (cognition, perception, action control, linguistics, and developmental science), perception, and systems.
4. Use of robots to motivate elderly to exercise and improve social interaction

O. Development of cognitive training applications/intervention to improve cognitive function in elderly

3. Rapidly develop novel, engaging computer-based cognitive training programs that are based on efficacious approaches and which use cognitive training to target a specific neural system/functional domain.
4. Augment existing computerized cognitive interventions to be personalized, engaging, adaptive, sufficiently challenging, and optimal for maximizing real world functional improvements.

Division of Neuroscience (DN)

A. Development of sensitive, specific and standardized tests for diagnostic screening of MCI and dementia; for example, the development of novel neuropsychological, biochemical and neuroimaging methods for the early detection of cognitive impairment and MCI and the early diagnosis of AD, and development of new tests for detection of pre-clinical AD.

B. Discovery, development, and/or evaluation of drugs, biological or natural products, including central-nervous-system delivery systems to remediate age-related cognitive decline, and to treat the cognitive impairment and/or behavioral symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of the disease or to prevent it entirely.

C. The development of practical applications using innovative technologies (e.g. hand-held, internet, telemedicine GPS, robotics, social networking and communications technologies) to support and improve quality of life, well-being, and the ability of people with MCI, AD or other dementias of aging to live independently and safely at home for an extended period of time. Examples include systems and devices to: evaluate, monitor and improve or adapt to changes in cognition; improve health service delivery; support independent living and the conduct of everyday tasks at home; provide information to health care providers and family members with which to evaluate the need for intervention; and promote communication and interaction between individuals living in the community or in institutional settings and their health care providers, friends and family members.

D. Testing in clinical trials of drug, nutritional, behavioral, cognitive or other types of interventions to remediate age-related cognitive decline, and to treat cognitive impairment and/or behavioral

symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of disease or to prevent the onset of disease.

E. Biosensors and prosthetic devices, technologies, and related software development to aid in the assessment, diagnosis, and remediation of age-related cognitive decline or sensory dysfunction (including pain, age-related vision loss, and age-related hearing loss), motor dysfunction (including Parkinson's disease and other motor disorders of aging), or age-related changes in balance, postural control, and gait. Novel markers of normal age-dependent cognitive decline or sensory and/or motor system changes at the molecular cellular, circuitry, physiological or behavioral level in humans or relevant animal models.

F. Improved technology for the analysis of structural and functional brain connectivity at the cell, neural circuitry and global network levels to define the normal trajectory of brain structure and function over the adult lifespan. Development of technology, including non-invasive methods and novel probes, to monitor and manipulate the plasticity of neural circuits in the adult and aged nervous system. Development of novel markers of neural stem cell function (proliferation, migration, and differentiation) as well as methods to assess the integration and function of stem cells in the nervous system.

G. Novel approaches for analysis of next-generation sequence data.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

Stem Cell Research for Alcohol-induced Disorders

A. Generate and disseminate induced pluripotent stem cells (iPS) from mature human cells to resemble diverse individual variations regarding alcohol metabolism. Use these genetic variant models to study alcohol dependence and pharmacotherapy development. Examples of these genetic variations include Alcohol Dehydrogenase (ADH), Aldehyde Dehydrogenase (ALDH), cytochrome P450 isozyme CYP2E1, and Glutathione S transferase (GST).

B. Generate and disseminate disease-specific iPS cell lines for studies on the biology and signaling pathways that contribute to the alcohol-related disease pathology.

C. Models derived from human iPS cells to study biological and pathological effects of alcohol and its metabolites.

In vivo detection of neuromodulators in behaving animals

A. Development and application of techniques that can detect neuromodulator changes in real time with spatial and temporal precision in behaving animals. Techniques that allow the *in vivo* detection of neuromodulators over an extended time period, such as implantable cell- or probe-based biosensors, will be particularly encouraged.

Ex vivo Efficacy Screens to Identify Pharmacotherapies for Alcohol Dependence

A. Development and validation of *ex vivo* screens capable of predicting efficacy test results in preclinical behavioral models of alcohol dependence. Such assays may include arrays of parameters capable of differentiating the alcohol dependent from the non-dependent state. They should also discriminate positive and negative control drugs found in the alcohol dependence pharmacotherapy literature and be sensitive to drugs with diverse mechanisms of action. In addition, the assays developed under this solicitation should be relatively rapid, simple and produce consistent and reliable results in multiple laboratories.

Develop Network Pharmacology Strategy for Preclinical Medication Development

A. Development of combined pharmacological approaches to synergistically regulate multiple drug targets for alcoholism. Areas that may be of interest to small businesses include, but are not limited to:

Objective 1: Develop and validate new target combinations using cellular and animal models.

Objective 2: Prioritize multi-drug targets and identify the effective drug combinations or multi-target drugs for the medication development.

Objective 3: Use high-throughput screening of compound libraries to identify multi-target drugs.

Objective 4: Encourage adaption of low throughput assays to high throughput screening, development of lead compounds, and identification of drug candidate(s) with proper pharmaceutical properties for medication development.

Novel tools and technologies to detect the effects of alcohol on the CNS structure and activities

A. Develop the novel tools and technologies to detect the effects of alcohol on activities of specific cell types, neuron-glia interactions, and the structure and activities of large numbers of neurons in alcohol-drinking/exposure settings, preferentially with intact neural network. These will include, but not limited to, the following:

1. Improving chemical or genetic sensors to detect dynamic changes in calcium, voltage, cAMP etc.
2. Developing tools and sensors to monitor structure and activities of neurons and glial cells, and their interactions
3. Developing tools and sensors to monitor synaptic activities
4. Defining cell types in the neurocircuits
5. Developing miniature and nanoscale apparatus and sensors, or miniaturizing and optimizing detection apparatus for the study of alcohol effects
6. Developing computational methods for the acquisition and analysis of large scale data

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

Division of Allergy, Immunology, and Transplantation (DAIT)

A. Development of novel vaccine adjuvants.

B. Development of medical countermeasures to protect against, mitigate, and treat the short- and long-term effects of radiation exposure due to terrorist attack.

C. Development of novel or improved decorporation agents to remove radionuclides from the body following accidental inhalation, ingestion or wound entry.

D. Identification of radiation exposure biomarkers and development of new biodosimetry methods and devices for triage of radiation-exposed people.

E. Novel approaches for detecting infants at risk for developing asthma and other allergic diseases.

F. Standardized validated diagnostic criteria and outcome measures for autoimmune diseases correlated with disease activity.

G. Innovative treatments for autoimmune diseases.

H. Methods and analysis tools to facilitate high throughput, high resolution MHC typing in humans and non-human primates

Division of Microbiology and Infectious Diseases (DMID)

A. Identify and qualify infectious disease-related biomarkers, including:

   1. Biomarkers to predict susceptibility to infection.
   2. Biomarkers to diagnose an infectious disease.
   3. Biomarkers to predict or monitor a subject's response to a therapeutic, including efficacy and toxicity biomarkers.
   4. Biomarkers to predict or monitor a subject's response to vaccination.
   5. Biomarkers to determine the possibility of infection mediated by insect vectors.
   6. Biomarkers from natural history studies that could be used to assess disease progression in acute and chronic diseases.

B. Development of more sensitive and accurate methods of direct detection of Borrelia burgdorferi for the purpose of diagnosing Lyme disease patients. Diagnostic approaches that contain one or more of the following are also encouraged: substantial and significant advances over conventional antibody-based approaches, methods that take into account host response, ability to detect and differentiate multiple strains of Borrelia burgdorferi, and discriminate between active and previous infection.

C. Vaccines for NIAID Category A, B, and C priority pathogens including influenza, Ebola, Marburg, arenavirus, and other viral encephalitides.

D. Vaccine development for tuberculosis, STIs, hepatitis B and C, and malaria and other high-impact global parasitic diseases.

E. Vaccine enhancement and formulation technologies with the goal of providing protection against multiple infectious disease agents, providing accelerated immune responses (more rapid schedules or reduced number of immunizations), increase ease of administration (i.e., self-administration), and increase product stability to minimize cold chain requirements.

F. Therapeutics for NIAID Category A, B, and C priority pathogens including smallpox, viral hemorrhagic fevers, viral encephalitides, botulinum neurotoxins, and influenza.

G. Therapeutics for tuberculosis, hepatitis B and C, and malaria and other high-impact global parasitic diseases.

H. Therapeutics exhibiting broad-spectrum activity against microbial pathogens.

I. Therapeutic enhancement and formulation technologies with the goal of improving drug development timeframes, productivity, efficacy, specificity, safety, stability, and delivery.

J. Development of simple, rapid, field-deployable, sensitive, and specific point-of-care in vitro diagnostics for:

- NIAID Category A, B, and C priority pathogens and those causing emerging and re-emerging infectious diseases.
- Respiratory disease pathogens including tuberculosis, community acquired pneumonia, and influenza, including emerging and re-emerging influenza viruses such as 2009 H1N1 influenza.

Division of AIDS (DAIDS)

A. Development of anti-HIV agents directed at new viral or cellular targets.

B. Development of novel anti-HIV drugs and therapeutics with focus on technological aspects such as multiplex analysis of drugs and innovative, streamlined methods for drug screening and drug delivery (e.g., multifunctional therapeutics based on nanotechnology). Development of bio-assay and bio-imaging applications for the assessment of HIV pathogenesis.

C. Preclinical development and evaluation of therapeutic vaccines and other immune-based therapies to attenuate HIV disease progression or reduce HIV infectiousness.

D. Development, standardization, validation and evaluation of improved technologies to detect HIV, to evaluate immune responses to HIV vaccines and to vaccine vectors, or to correlate immune responses associated with vaccine efficacy.

E. Development and evaluation of practical and affordable tests to measure viral load, CD4+ cell counts, and drug toxicities and drug resistance to monitor populations in resource-poor settings. Development of tests to detect early infection in seropositive HIV-infected individuals.

F. Discovery and development of agents or strategies for Pre-exposure prophylaxis (PrEP) (single or multiple agents, immunological, pharmacological, or other potential approaches directed against viral and/or host targets). Development of pharmacological tools to examine PK/PD in fluids and tissue, new formulation and delivery systems (including nanotechnology-based approaches) for coitally-dissociated use, and optimization of animal models for screening of candidate agents.

G. Development of novel and improved assays for the determination of HIV incidence. These diagnostic assays should identify HIV infection before seroconversion, be based on B and non-B subtypes, and include the development, incorporation, and validation of process controls.

H. Development of rapid tests for the detection of ARTs in various human matrices (e.g. blood, urine, hair). The assay should require minimal operator effort and expertise, and include the development, incorporation, and validation of process controls.

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

A. Research and development of new therapies using small molecules or biologics for arthritis, musculoskeletal and skin diseases.

B. Research and development of novel biomedical devices or tissue engineered products for arthritis, musculoskeletal and skin diseases.

C. Research and development of new biomarkers or novel imaging technologies for arthritis, musculoskeletal and skin diseases.

D. Research and development of innovative internet-based technologies to manage arthritis, musculoskeletal and skin diseases.

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)

A. ***Image-Guided Interventions.*** Research on use of images for guidance, navigation and orientation in minimally invasive procedures to reach specified targets. Examples include image-guided interventions for minimally invasive therapies such as surgery and radiation treatment, for biopsies, and for the delivery of drugs, genes and therapeutic devices.

B. ***Magnetic Resonance Imaging and Spectroscopy.*** Development of MR imaging and MR spectroscopic imaging, for both animal and human research, and potential clinical applications. Examples include (but are not restricted to) fast imaging, high field imaging, design of novel RF and gradient coils, novel pulse sequences, design of novel contrast mechanisms, imaging informatics, *in vivo* EPR imaging, molecular imaging, etc. The emphasis should be on technological development rather than detailed applications to specific diseases or organs.

C. ***Medical Devices and Implant Science.*** Design, development, evaluation and validation of medical devices and implants. This includes exploratory research on next generation concepts for diagnostic and therapeutic devices; development of tools for assessing host-implant interactions; studies to prevent adverse events; development of predictive models and methods to assess the useful life of devices; explant analysis; improved *in vitro* and animal models for device testing and validation.

D. ***Micro- and Nano-Systems, Platform Technologies.*** Development of BioMEMS, microfluidics and nanoscale technologies, including micro-total analysis systems, arrays, and biochips, for detection and quantitation of clinically relevant analytes in complex matrices. Application areas include biomedical research, clinical laboratory diagnostics, biodefense, high-throughput screening, drug delivery, tissue engineering, and implantable devices, among others.

E. ***Optical Imaging and Spectroscopy.*** Development and application of optical imaging, microscopy, and spectroscopy techniques; and development and application of optical imaging contrasts. Examples of research areas include fluorescence imaging, bioluminescence imaging, OCT, SHG, IR imaging, diffuse optical tomography, optical microscopy and spectroscopy, confocal microscopy, multiphoton microscopy, flow cytometry, development of innovative light sources and fiber optic imaging devices.

F. ***Telehealth.*** Development of software and hardware for telehealth studies that have broad applications as well as early stage development of telehealth technologies that may have specific focus areas. Research that is supported includes methods to address usability and implementation issues in remote settings, and methods to develop technology for standardizing and incorporating state of the art security protocols for verifying user identities and preserving patient confidentiality across remote access.

G. ***Tissue Engineering and Regenerative Medicine.*** Development of enabling technologies including real-time, non-invasive tools for assessing the function of engineered tissues; real-time assays that monitor the interaction of cells and their environment at the molecular and organelle level; predictive computational models for engineering function 3D tissues; high-throughput assays and instruments to reduce the cost, time, and complexity of tissue engineering; novel bioreactor techniques for expanding stem cells and growing tissues and organs on a large scale; and strategies for preserving, sterilizing, packaging, and transporting living-tissue products. The program also supports applications of rational engineering design principles to functional engineered tissues; the development of novel biomaterials for use as tissue scaffolds that mimic the extracellular matrix and support multiple cell types in defined spatial orientation; and engineering approaches to study how biomaterials interact with cells and guide cell growth, differentiation, and migration.

H. ***Ultrasound.*** Improvement of technologies for diagnostic, interventional and therapeutic uses of ultrasound. The diagnostic ultrasound program includes, but is not limited to the design, development and construction of transducers, transducer arrays, and transducer materials, innovative image acquisition and display methods, innovative signal processing methods and devices, and optoacoustic and thermoacoustic technology. It also includes the development of image-

enhancement devices and methods, such as contrast agents, image and data presentation and mapping methods, such as functional imaging and image fusion. The interventional ultrasound program includes the use of ultrasound for therapeutic use, or as an adjunct for enhancement of non-ultrasound therapy applications. Examples include, but are not limited to, high-intensity focused ultrasound (HIFU) as a non-invasive or minimally invasive interventional surgical or therapy tool, and as an adjunct interventional tool. It also includes the use of ultrasound contrast agents for therapy and for targeted drug delivery, and the use of ultrasound for image-guided surgery, biopsy, and other interventions.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

Developmental Biology and Structural Variation Branch

A. Innovative technologies for imaging developmental processes and gene expression

Fertility and Infertility Branch

A. Development of improved technologies for the reprogramming of cells, including embryonic stem cells or adult cells, into eggs and sperm.

Maternal and Pediatric Infectious Disease Branch

A. New technologies relevant to resource-limited countries for:
   1. diagnosis of HIV infection and other infectious diseases in infants;
   2. diagnosis and treatment of HIV-related complications of HIV (e.g., diagnosis of tuberculosis in children);
   3. simple and less technical point of care assays to monitor CD4 cell percentage/count, HIV viral load, or other surrogate markers of HIV disease progression in children.

Obstetric and Pediatric Pharmacology and Therapeutics Branch

A. Development of nanosized formulations to optimize efficacy and minimize toxicity of pediatric drugs

Pediatric Growth and Nutrition Branch

A. Technological innovations/inventions to diagnose and monitor diabetes

Pediatric Trauma and Critical Illness Branch

A. Research and development of devices and innovative therapeutic technologies for management of physical disabilities and related problems stemming from and acute injuries

Population Dynamics Branch

A. Technological innovations or inventions to improve collection of biomarker data in large population-representative surveys.

Pregnancy and Perinatology Branch

A. Devices, instruments, and tools to minimize bacterial colonization, reduce proclivity for thrombous formation; reduce health-care associated infection risks.

National Center for Medical Rehabilitation Research

A. Novel Technology – Using nanomaterials, biomarkers, imaging, and robotics. to improve rehabilitation treatment for restoration of function. Develop techniques to improve/maximize parameters for trans-cranial magnetic stimulation.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)

A. Research and development for biomedical technologies (medical devices, instruments, pharmaceuticals, drugs, therapeutics, vaccines, diagnostics and biologics) that require regulatory approval by the FDA before the final product could be sold for technology within the NIDCD mission.

Hearing and Balance Program

A. Development of neural prostheses to treat specific neural deficits

Voice, Speech, and Language Programs

A. Development of new systems of communication for individuals with motor speech impairment, including a brain computer interface (BCI) communication prosthesis

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)

Infectious Diseases and Immunity

A. Develop oral topical formulations with combined microbicidal, analgesic, and anti-inflammatory activities to enhance oral mucosal defenses and prevent and/or control oral infections and lesions in HIV-infected and/or immunosuppressed subjects.

Clinical Research

A. Develop improved methods to detect and predict progression of dental caries, periodontal disease, reversible pulpitis and irreversible pulpitis.

B. Improve or develop new methods to enhance oral and craniofacial surgery. This would include both intraoral and extraoral surgery.

C. Develop improved methods to mechanically repair or treat tooth structure damaged by dental caries or periodontal disease.

Oral, Oropharyngeal and Salivary Gland Cancers

A. Develop regimens for the alleviation of the oral complications of cancer therapy.

Temporomandibular Joint Disorder and Orofacial Pain

A. Discovering and developing novel, pharmacological medications for treating chronic orofacial pain disorders, by leveraging results from ongoing genetic studies of chronic pain conditions

Saliva, Salivary Diagnostics, and Salivary Gland Diseases

A. Development of viral, non-viral and gene therapy-based approaches to address compromised salivary gland function. Development of cell and tissue-based strategies and technologies for restoration of damaged or destroyed salivary gland function.

B. Development of novel compounds or materials that protect and preserve salivary glands from head and neck cancer irradiation therapy.

C. Development of non-invasive methods for the determination of efficacy and safety of artificial saliva, sialogogues, and of their delivery vehicles used in addressing the diminution or lack of saliva (xerostomia) due to Sjögren's Syndrome or head and neck cancer irradiation therapy.

D. Development of immunological strategies and immunotherapy-based approaches for addressing xerostomia from Sjögren's Syndrome.

Biotechnology, Biomaterials, and Applications for Regeneration and Restoration of Oral, Dental and Craniofacial Tissues

A. Development of methods, materials, and devices for orthodontic, prosthetic, and craniofacial applications including those that can be used for craniofacial bone distraction, craniofacial reconstruction, healing, and scarless repair.

B. Development of imagining diagnostics to accelerate clinical implementation of reliable, reproducible, highly specific and sensitive diagnostic instruments for dental caries, cracked teeth, pulp vitality, bone quality, and periodontal diseases.

Clinical and Behavioral Research

A. Develop and test for safety, efficacy, and/or effectiveness of measures or materials for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

Diabetes, Endocrinology and Metabolic Diseases

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. NIDDK will give priority to research that has already progressed to an *in vivo* model or to be clinically tested.

B. Develop telemedicine approaches that can be incorporated as components/and or adjuvants of an artificial pancreas for better diabetes self-management.

II. SCREENING TESTS, DIAGNOSTICS AND BIOLOGIC TOOLS:

A. Development of techniques or products useful for predicting, preventing or delaying progression of diabetes, including tests for identifying patients at risk, and methods of monitoring disease progression.

B. Development of diagnostic tools to measure the autonomic neuropathy that develops in people with diabetes.

C. High throughput - Point of care technologies (reliable, accurate, cost-effective, highly sensitive, standardized having rapid turnaround time) for autoantibody detection, T cell –subsets-auto-reactivity and other immune parameters for autoimmune diabetes diagnosis and follow-up.

D. 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.

E. 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.

F. Point of care low cost /portable technologies for diabetes and pre-diabetes diagnosis

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 or devices to prevent and treat diabetic foot ulcers.

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 utilizing replenishable cell sources, especially stem cells that produce functional islet like cells/tissues that can be successfully transplanted.

E. 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.

F. Development of novel technologies that may facilitate self management of diabetes and adherence to treatment.

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.

Digestive Diseases and Nutrition

I. Digestive and Liver Diseases (Clinical)

A. Development of assays and new genetic screening methods for detection of biomarkers for genetic predisposition to GI-relevant diseases, e.g., IBD, hemochromatosis, Wilson's disease.

B. Development of improved means for detecting Barrett's esophagus.

C. 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).

D. Development of novel antifibrotic therapies for progressive liver failure.

E. Development of quantitative tests of hepatic "reserve" which would be of use, for example, in assessing the risk of surgery in patients with liver disease.

F. Develop and validate therapeutic interventions for treatment and/or progression of pancreatitis and its complications.

G. Develop gastrointestinal endoscopic instruments that have improved visualization and therapeutic capabilities for detecting mucosal abnormalities and pathologies and providing improved interventional capabilities.

II. Digestive and Liver Diseases (Basic)

A. Development of new techniques, including non-invasive imaging, to measure motility/intestinal transit at various sites within the gastrointestinal tract.

B. Development of techniques for the preservation and transplantation of small intestine and pancreas.

C. 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.

D. Development of non- or minimally-invasive devices/ techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.

E. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

F. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.

G. Development of humanized mouse models of multi-allelic diseases.

H. Development of novel proteomic or metabolomic technologies designed to study digestive and liver diseases, and their complications.

I. Development of biomarkers or imaging methods that quantitatively measure hepatic regeneration.

J. Development of biomarkers that quantitatively assess the degree of cold and warm ischemia injury in donor liver organs.

III. Nutrition, Obesity, and Eating Disorders

A. Development of a non-invasive breath or blood test to accurately measure dietary intake.

Kidney, Urologic and Hematologic Diseases

I. Application of Proteomics and Metabolomics to Kidney, Urologic and Hematologic Diseases

A. Identification or development of novel proteomic or metabolomic technologies designed to study kidney, urologic, or hematologic diseases.

II. Kidney

A. Development of pharmacological agents that might be used to intervene in acute or chronic renal disorders and in disorders of renal hemodynamics, blood pressure, electrolyte metabolism, and extracellular volume regulation.

B. 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).

C. Development of material(s) for construction of urinary catheters that may reduce the incidence of infection in the urinary tract, and materials that decrease uretheral and bladder inflammation due to foreign body.

D. Development of early diagnostic tools, preventative measures, and treatment modalities for acute kidney injury.

E. Development of new non-invasive methods for measuring kidney function:

   1. Development of new biomarkers for early detection of kidney dysfunction, prediction of progression, and early indication of recovery.

III. Urology

A. Development of diagnostic modes to clinically non-invasively or minimal-invasively measure bladder obstruction before and after surgical or pharmaceutical intervention and/ or treatment devices for bladder outlet obstruction.

B. Development of localization methods through imaging or non-invasive methods or instrumentation using minimally-invasive methods to access stones for therapy. Methods to directly improve access to difficult stones.

C. Development of more real-time diagnostic assessment of lower urinary tract function using non-invasive, remote or minimally invasive measures, which can include neuro-pharmacological/neuro-physiological assessments in urodynamics.

D. Development of non-invasive or minimally invasive treatment methods or pharmacological for urinary incontinence and/or bladder instability.

E. Non-invasive, reduced or non-radiological diagnostic methods for evaluating vesico-ureteral reflux in children and infants.

IV. Hematology

A. Development of methods and equipment for routine high volume isolation of highly purified hematopoietic stem and progenitor populations.

B. Development of chemically defined reagents that support hematopoietic stem cell proliferation and differentiation.

C. Development of non-invasive systems for monitoring the total hemoglobin and hematocrit, suitable for use with adults or neonates.

D. Development of new methods for the non-invasive or minimally invasive measurement of body iron.

E. Design of therapeutic drugs for inducing fetal hemoglobin synthesis.

F. Design and validation of novel therapeutic agents that modulate hepcidin and cellular ferroportin expression and/or activity *in vivo*.

NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

A. Drug discovery and development-enabling activities: Development of innovative technologies, methods or tools, including but not limited to:

1. Innovative in vitro, in situ, or in vivo tools for the molecular analysis of the central nervous system, normal and/or diseased.
2. Tools to simplify drug design through the use of advanced computing (simulation) methods.
3. Development of pre-clinical models for addiction.
4. Creation of a data repository / software tools for addiction-related clinical research data.
5. Novel analytical technologies and methods that enhance the understanding of basic mechanisms of drug action and improve drug testing; technologies designed to overcome the performance limitations of current drug discovery and development tools.
6. Technologies, including molecular imaging, gene expression profiling, and genotyping and sequencing approaches designed to better inform the diagnosis and treatment of substance use disorders

B. Drug discovery and development activities: Application of emerging and existing technologies and platforms to Substance Use Disorder (SUD) drug development. Medical products with potential to minimize drug seeking, compulsive behavior, and/or addictive processes are strongly encouraged. Examples might include, but are not limited to:

1. Chemistry / pharmaceutical drug development
2. Formulation and/or enhanced delivery of drugs
3. Preclinical and/or clinical drug development
4. Development of biomarkers related to treatment outcomes

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

Division of Cell Biology and Biophysics

A. Development of instrumentation, devices, and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.

B. Development of new methods and materials directed toward the solution of biological macromolecule structures, including membrane proteins, assemblies and complexes by, but not limited to, x-ray diffraction, electron diffraction, NMR and mass spectroscopy.

C. Imaging probes and sensors, other reagents and methods, instrumentation, software for microscopy, spectroscopy, and single molecule analysis of molecules, cells, tissues, embryos and small model organisms. Technologies for applications of microscopy, spectroscopy and single molecule analysis in basic biomedical research, including but not limited to light, electron, X-ray and scanning probe microscopy and fluorescence, magnetic and electron paramagnetic spectroscopy. NOT included are small animal and preclinical imaging and high throughput platforms for diagnostic and clinical applications.

Division of Genetics and Developmental Biology

A. Development of probes for detection of human genetic polymorphisms, including disease genes.

B. Development of valid animal models for genetic diseases and birth defects.

C. Development of tools and technologies to detect and monitor complex human phenotypes or traits.

D. Development or improvement of methods for high throughput detection of epigenomic changes.

E. Development or improvement of methods for characterizing the metabolic interactions of complex communities of microorganisms particularly those involved in host-microbe interactions.

F. Development of improved or novel methodology for structure/function analysis of very large macromolecular complexes involved in transmission or expression of genetic material.

Division of Pharmacology, Physiology, and Biological Chemistry

A. Methods for isolation, characterization, and production of natural and bio-engineered products.

B. Isolation, characterization, and development of factors and strategies, methods, or treatments involved in tissue repair, wound healing, sepsis, and traumatic injury, emergency, peri-operative, or critical care conditions, and associated pain management.

C. Research to improve drug design and delivery.

D. Research to discover, detect, and understand the genetic basis of individual differences in drug responses (pharmacogenomics).

E. Development of novel *in vivo* and *in vitro* methods to predict the safety and toxicities of pharmacologic agents.

F. Development of methods and tools for the field of glycomics including but not limited to development of: specific glycan structural databases, methodologies for synthesis of robust glycan libraries, glycan labeling reagents and glycol-enzyme inhibitors, analytical tools for determining carbohydrate structure abs assessing its biological function.

Division of Biomedical Technology, Bioinformatics, and Computational Biology

A. ***Technology for Structural Biology:*** Development of detectors and cameras for studying the structures of biomolecules in the size range of peptides to cells, using synchrotron radiation and multiple types of microscopy and spectroscopy.

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

All divisions:

A. Preclinical drug/device development studies, including pharmacology, efficacy and toxicology.

B. Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.

C. Studies in normal healthy volunteers to determine a drug's safety profile, metabolism, etc.

D. Clinical studies in patient/disease population to assess the drug's effectiveness.

E. Assessment of devices with regard to performance standards related to the FDA approval process.

F. Safety and effectiveness studies of novel medical devices.

G. Evaluation of novel imaging approaches for diagnostic purposes.

H. Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

I. Rapidly develop novel, engaging computer-based cognitive training programs that are based on efficacious neurotherapeutic approaches and which use cognitive training to target a specific neural system/functional domain.

J. Augment existing computerized cognitive interventions to be personalized, engaging, adaptive, sufficiently challenging, and optimal for maximizing real world functional improvements.

K. Test the feasibility, efficacy and potential adverse effects of these programs utilizing measures of functional outcomes in an identified clinical population, particularly those with neuropsychiatric disorders, ASD, and/or HAND, at a specified developmental stage, including measurement of the duration of treatment effects.

Division of Neuroscience and Basic Behavioral Science (DNBBS)

A. Novel imaging probes to study brain structure and function at all levels, from the molecular to the whole organ, using any imaging modality (PET, fMRI, optical, etc.).

B. Drug discovery/drug development of novel compounds which act on molecular pathways (receptors, enzymes, second messengers, etc.) that are not typically targeted with currently available psychiatric drugs, and that have a strong biological justification as a novel mechanism for treatment of psychiatric disorders.

C. Novel screening assays for high throughput acquisition and analysis of data about behavior and the brain, from the level of genes to the level of behavior.

D. Novel technologies that would enable researchers to study how populations of neural cells work together within and between brain regions, in order to understand how changes in neural activity contributes to mental disorders.

E. Novel informatics tools to facilitate the sharing of complex data sets between laboratories.

F. Novel tools for investigating brain-derived GPCRs in mental health research.

Division of Developmental Translational Research (DDTR)

A. Develop, test and validate reliable and stable biomarkers that can identify at-risk individuals prior to disease onset, improve diagnosis, predict treatment response, or measure disease progression. Biomarkers are also needed in clinical trials to identify dose ranges, to identify a specific subpopulation of subjects to enroll in a treatment trial, or to measure efficacy or toxicity/side effects.

B. Develop novel and targeted interventions (pharmacological, cognitive, behavioral, computer, or device-based) that affect particular neural circuits and signaling pathways relevant to the developmental trajectory of the disease.

C. Based on expanded knowledge of neurobehavioral trajectories, develop novel objective assessment tools that can identify early signs of risk or onset of recurrence of particular mental disorders or in domains of functioning (see MH's RDoC project: http://www.nimh.nih.gov/research-funding/rdoc/index.shtml) for pediatric populations.

D. Develop computational behavioral assessment tools that can be used across ages, species, and cultures to evaluate dysfunction in domains relevant to mental disorders (e.g., mood dysregulation, deficits in executive function).

E. Develop computational platforms to enable the integration and sharing of data characterizing typical and atypical developmental trajectories in humans and non-human animals.

F. Clinical research tools.

Division of Adult Translational Research and Treatment Development (DATR)

A. Develop valid measures of the various constructs in the Research Domain Criteria (RDoC) matrix (see http://www.nimh.nih.gov/research-funding/rdoc/index.shtml), e.g., neurocognitive tasks, psychometrically sophisticated questionnaires, measures of behavior, and biomarkers, into a commercial product.

B. Conduct early stage, proof of concept clinical trials to advance the development of novel therapeutics. The clinical trials are expected to include biological/behavioral data to assess target engagement and to help determine potential success or failure of the compound before moving on to larger clinical trials (see NOT-MH-11-015 http://grants.nih.gov/grants/guide/notice-files/NOT-MH-11-015.html).

C. Develop, test and validate reliable and stable biomarkers that can identify at-risk individuals prior to disease onset, improve diagnosis, predict treatment response, or to measure disease progression. Biomarkers are also needed in clinical trials to identify dose ranges, to identify a specific subpopulation of subjects to enroll in a treatment trial, or to measure efficacy or toxicity/side effects.

D. Develop clinical risk assessment instruments that encompass multiple domains (e.g., genetic, neurobiological, and environmental), are sensitive to developmental stage, and have high predictive power for the onset or recurrence of mental illness.

E. Develop novel and targeted interventions (pharmacological, behavioral, or devices) that affect particular neural circuits and signaling pathways relevant to the developmental trajectory of the disease.

F. Develop electronic sensors, monitoring devices and systems, and data analysis software for automated detection and diagnosis of mental disorders and key transdiagnostic dimensions of psychopathology.

G. Develop risk assessment measures, methods and paradigms capable of evaluating individualized risk for developing mental disorders, or for developing particular benefits or harms during treatment for mental disorders, and communicating such probabilistic information to patients and their families in a readily understandable manner.

H. Clinical research tools.

Division of AIDS Research (DAR)

A. Develop and test novel, non-invasive diagnostic approaches (instrumentation, imaging, biomarkers, central nervous system [CNS] cell-based *in vitro* models) to detect neurocognitive dysfunction associated with HIV-1 infection and innovative technologies to study the mechanisms involved in HIV-

1 associated neuropathogenesis and persistence of HIV-1 in the CNS. or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy

B. Design and test novel therapeutic strategies aimed at amelioration of HIV-1 associated neurocognitive disorders (HAND) and eradication of HIV-1 from CNS reservoirs or strategies to prevent viral resurgence in the CNS upon cessation of anti-retroviral therapy.

C. Discover and develop innovative technologies for targeting therapies to the brain, including antiretroviral drugs, nanotechnology, imaging tools to study HIV-aging interactions or HIV-related neurodegeneration and neuroprotective strategies with improved capability to cross the blood-brain barrier for amelioration of HAND.

D. Design new strategies to reduce adverse effects of anti-retroviral drugs such as neuropsychiatric side effects and drug-drug interactions.

E. Develop or adapt neurological/neuropsychological/neurobehavioral assessments to evaluate HIV-1 associated abnormalities in adults or children in resource poor environments that are adaptable to different cultures and languages.

F. Develop innovative approaches to improve the scientific assessment of HIV sexual risk behavior through remote sensing devices, biomarkers, or other novel methods.

G. Develop and test tools, curricula, and strategies that seek to reduce documented racial/ethnic, gender, and age-related disparities in HIV infection or in HIV treatment adherence and treatment outcomes.

H. Develop novel tools and approaches to identify, recruit, enroll, and/or retain those most vulnerable to HIV/AIDS (e.g., African-American MSM, adolescents) in HIV prevention research and/or initiatives.

I. Develop and test tools, curricula, or other approaches designed to facilitate the effective implementation of emerging biomedical HIV prevention methods (e.g., pre-exposure prophylaxis, microbicides, circumcision, etc.), including but not limited to approaches that address behavioral aspects of biomedical prevention (e.g., provider knowledge and training; patient uptake, adherence, HIV screening, and risk-reduction counseling; adverse event monitoring, etc.).

J. Develop or adapt and evidence-based HIV sexual risk reduction, psychosocial coping, or treatment adherence interventions for delivery through the internet or mobile devices, with the aim of expanding intervention access, fidelity of delivery, and/or intervention tailoring.

K. Develop novel tools and approaches designed to improve HIV treatment outcomes by rapidly linking individuals diagnosed with HIV to primary medical care, enhancing patient readiness for initiation of antiretroviral medications, improving and sustaining patient adherence to antiretroviral medications, and/or improving patient retention in medical care.

L. Develop innovative approaches designed to improve the quality of HIV testing, (including rapid home based HIV antibody tests), HIV counseling, prevention, and treatment services by strengthening patient-provider communication and/or modifying the decision-making processes and practice behaviors of health care providers.

M. Develop innovative approaches designed to improve the uptake and understanding of rapid home based HIV antibody tests by key populations at higher risk for HIV as well as innovative interventions that can be paired with home test kits to increase linkage and engagement in HIV care for those testing positive.

N. Develop novel information technology tools designed to improve dissemination of evidence-based interventions and assist healthcare providers, community-based organizations, and professional or advocacy organizations in identifying, adopting, and implementing proven HIV prevention and treatment interventions.

Division of Services and Intervention Research (DSIR)

A. Randomized clinical trials evaluating the effectiveness of known efficacious interventions.

B. Analyses of naturalistic databases to evaluate the effectiveness of known efficacious interventions.

C. Identifying moderators and mediators of intervention effects as a step to design and test personalized interventions.

D. Evaluating the combined or sequential use of interventions.

E. Determining the optimal length of intervention, establishing the utility of continuation or maintenance treatment (that is, for prevention of relapse or recurrence).

F. Evaluating the long-term impact of efficacious interventions on symptoms, functioning, and quality of life.

Services research covers all mental health services research issues across the lifespan and disorders, including but not limited to:

A. 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).

B. Interventions to improve the quality and outcomes of care.

C. Enhanced capacity for conducting services research.

D. The clinical epidemiology of mental disorders across all clinical and service settings.

E. The dissemination and implementation of evidence-based interventions into service settings.

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES (NIMHD)

A. Telehealth technologies for remote diagnosis and monitoring.

B. Telemedicine to improve access to specialty care which would normally not be accessible because of high cost and transportation. This would also link up academic tertiary-oriented health centers with community-based primary care homes.

C. Use of currently available technology (e.g. phone lines, televisions with remote controls, cellphones, weight scales, diabetic glucometers, thermometers) within underserved settings to provide self-management and patient education, increase patient-clinician communication and surveillance of chronic disease conditions.

D. Improved early detection (via saliva testing, breath testing, blood testing) of diseases where there are significant health disparities.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The NINDS accepts a broad range of small business applications that are significant, innovative, and relevant to its mission. Examples of research topics within the mission of NINDS are shown below. This list is not all inclusive and some research areas fall into multiple categories.

1. Therapeutics and Diagnostics Development for Neurological Disorders, including biomarker and diagnostic assays, therapeutics (drugs, biologics, and/or devices) for treatment of neurological disorders, and technologies/methodologies to deliver therapeutics to the nervous system.
2. Clinical and Rehabilitation Tools, including intraoperative technologies for neurosurgeons, rehabilitation devices and programs for neurological disorders, and brain monitoring systems
3. Technology and Tools, including technologies to image the nervous system, neural interfaces technologies, and tools for neuroscience research and drug development.

Within these research topics, the following research may require additional funds above the hard budget caps:

A. *In vivo* animal testing required for therapeutics and diagnostics development.

B. Drug and biologics preclinical discovery and development activities for regulatory submission, such as lead identification/optimization, preclinical efficacy testing, IND-enabling studies, and manufacturing for clinical trials.

C. Device preclinical discovery and development activities for regulatory submission, such as hardware prototyping, device/software verification, biocompatibility/sterilization testing, pre-clinical efficacy testing, large animal GLP safety testing, and preparing material/devices for human testing.

D. Clinical testing of therapeutics (drugs, devices, or biologics), diagnostics, clinical and rehabilitation tools (i.e. intraoperative technologies, rehabilitation devices and programs, and brain monitoring systems), and technologies for clinical research. This would include clinical research studies to test scientific hypothesis that are not feasible or practical to conduct in animal models but would inform a final device design.

E. *In vivo* animal testing of technologies for animal research and development of animal models for drug development and neuroscience research.

F. Research that requires special facilities to contain hazardous or infectious materials.

DIVISION OF PROGRAM COORDINATION, PLANNING, AND STRATEGIC INITIATIVES (DPCPSI), OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS (ORIP)

Research and Development in Comparative Medicine

A. Development of new technologies to rapidly phenotype large number of animals.

B. Development of technologies to identify biomarkers for clinical diagnostics in well validated disease models.

C. Development of vaccines and new therapeutic agents to prevent and/or control selected laboratory animal diseases. One high priority need is to develop methods to control and prevent Herpes virus B in nonhuman primates.

D. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control and operational efficiency, including improvements in caging and remote monitoring in animal facilities.

E. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies of various human diseases, excluding most random mutagenesis projects performed on rodents.

F. Development and refinement of high throughput technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.

G. Development of improved reagents, techniques, and equipment to perform, analyze, capture and process data gathered in “omics” studies (genomics, transcriptomics, phenomics, proteomics, glycomics, epigenomics, metabolomics) in normal and disease-condition animal models.

H. Development of biological tools and reagents for reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease. Development of the technologies and procedures to test efficacy and safety of these experiments in animal models. Approaches to detect and track the implanted cells and tissues *in vivo*.

I. Development of new technologies in animal/cell models to study the function (activation/silencing) of noncoding DNA or RNA regions in the development of diseases.

J. Development of acellular biomaterials, biosensors and reagents to promote, detect and track reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease.

Other Research Topic(s) within the Mission of the Office of Research Infrastructure Programs

A. Development of methodologies, diagnostics, technologies, equipment, assay systems and portable devices that can be used in community settings, such as health centers, neighborhood clinics, doctor offices, public schools, libraries, and rural and remote locations to facilitate biomedical and behavioral research;

B. Development of culturally appropriate educational materials for student, teacher and community health literacy and disease prevention/intervention such as: software, videos, printed material to facilitate translation and dissemination of evidence-based health information; and

C. Innovative applications of health information technology, including telemedicine/telehealth tools and technologies, to facilitate electronic health information exchange, enable clinical research at the point of care, and improve access to quality health care for hard to reach populations.