

BIOENGINEERING APPROACHES TO ENERGY BALANCE AND OBESITY (SBIR/STTR)

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Department of Health and Human Services (DHHS)

PARTICIPATING ORGANIZATION:

National Institutes of Health (NIH)  
(<http://www.nih.gov>)

COMPONENTS OF PARTICIPATING ORGANIZATION:

National Heart, Lung, and Blood Institute (NHLBI)  
(<http://www.nhlbi.nih.gov>)

National Institute of Biomedical Imaging and Bioengineering (NIBIB)  
(<http://www.nibib.nih.gov>)

National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK)  
(<http://www.niddk.nih.gov>)

National Cancer Institute (NCI)  
(<http://www.nci.nih.gov>)

National Institute on Aging (NIA)  
(<http://www.nia.nih.gov>)

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APPLICATION RECEIPT DATE(S): Applications submitted in response to this program announcement will be accepted at the standard application deadlines (April 1, August 1, December 1) through August 1, 2007.

THIS PA CONTAINS THE FOLLOWING INFORMATION:

- o Purpose of the PA
- o Research Objectives
- o Mechanism(s) of Support
- o Project Period and Amount of Award
- o Eligible Institutions
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NOTICE: This program announcement (PA) must be read in conjunction with the current Omnibus Solicitation of the National Institutes of Health, Centers for Disease Control and Prevention, and Food and Drug Administration for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR)

Grant Applications. The solicitation (see <http://grants.nih.gov/grants/funding/sbirsttr1/index.pdf> [PDF] or <http://grants.nih.gov/grants/funding/sbirsttr1/index.doc> (MS Word)) contains information about the SBIR and STTR programs, regulations governing the programs, and instructional information for submission. All of the instructions within the current SBIR/STTR Omnibus Solicitation apply.

#### PURPOSE OF THE PA

The purpose of this PA is to solicit applications to develop and validate new and innovative bioengineering technology to address clinical problems related to energy balance, intake, and expenditure. Novel sensors, devices, imaging, and other approaches are expected to be developed and evaluated by collaborating engineers, physical scientists, and scientists from other relevant disciplines with expertise in obesity and nutrition. The goal is to increase the number of useful technologies and tools available to scientists to facilitate their research in energy balance and health. Eventually these research tools should facilitate therapeutic advances and behavioral changes to address such problems as weight control and obesity.

#### RESEARCH OBJECTIVES

##### Background

##### Public health need

Obesity is a problem of energy balance, wherein adipose tissue stores accumulate to excess levels when expenditure does not keep up with intake. At present, approximately 65% of American adults are either overweight ( $\geq 25$  kg/m<sup>2</sup>) or obese ( $\geq 30$  kg/m<sup>2</sup>), and approximately 15% of American children are similarly categorized (by age-adjusted percentiles of weight for height). This situation reflects the high-energy efficiency of American life, where little physical effort is needed for work and recreation, and where the national diet is abundant in low-cost, energy-dense food. Popular approaches to weight control have been generally unsuccessful, despite constant publicity about the problem and considerable individual efforts at weight loss.

The health consequences of obesity (e.g., diabetes, cancer, heart disease) are predicted to grow worse. Type 2 diabetes rates are rising in adults and children, and a substantial increase in morbidity and mortality from cardiovascular disease

is expected. Furthermore, obesity has been linked to the development of several types of cancer. Ultimately, resolution of the obesity epidemic at the population level will depend on individual behavioral change that takes place within the larger societal environment. Such changes may be facilitated through better medical therapies. However, technologies and tools to more easily monitor behavior and achieve treatment goals are also needed.

Conversely, inadvertent weight loss (cachexia) is also of high concern, particularly in the aging population. Cachexia represents a situation of persistent negative energy balance that often is accompanied by disproportionate loss of muscle tissue, weakness, and steady deterioration of physical function. Aged individuals are less likely than younger persons to be able to restore body weight after a period of impaired intake, perhaps due to aging-related blunting of compensatory effects on appetite. Overall, little is known about how best to reverse cachexia once it develops; methods for detecting the onset of such periods would be useful. Cachectic states also are common among patients with advanced stages of chronic diseases such as heart failure, chronic obstructive pulmonary disease, and cancer.

Aging poses additional interesting questions related to energy balance and its assessment. When studying these, one must distinguish between the normal biology of aging, as opposed to age-associated ailments that are part of the health and social experience of the aged population. Even relatively healthy, high functioning individuals will experience age-related declines in metabolic rate, muscle mass, energy intake, energy expenditure. However many aged individuals are characterized by existing poor function, an ever-increasing propensity to adverse unpredictable events (such as falls and sudden illness), and impaired response to such events. Prediction of the propensity to such events, and detection of early stages of impaired adaptive responses, is needed in order to preserve functional capacity.

Clearly, the ability to measure states of energy balance and its various components, such as dietary intake, resting metabolism, and physical activity, is a critical public health need. However, this is remarkably difficult to achieve in satisfactory fashion, and the inconvenience, expense, and relative inaccuracy

of current methods are a persistent and serious barrier to progress. Engineering approaches have the potential to overcome these limitations, but represent a relatively untapped area of scientific expertise for tackling the research issues and practical aspects of the obesity epidemic. Emerging technologies, such as nanotechnology, also offer unique opportunities for interfacing with engineering approaches to help address some of the problems in obesity research.

#### Challenges in measuring energy balance

Assessment of human energy balance, the net difference between energy intake (by diet) and expenditure (by work and heat), is a key component of obesity research, prevention, and treatment. The importance of accurate measurement of states of energy balance can be appreciated by considering average weight gain in middle-aged adults (~10 lb/decade). This significant gain in weight results from very small, persistent excesses of intake over expenditure of approximately 0.3% of the daily calorie consumption. This imbalance is well below the level of perception for most individuals. Similarly, energy expenditure from physical activity must be quantified accurately in order to understand the dose effects of exercise on body weight and other aspects of health, such as blood pressure. Weight loss programs often include ~5% increments of expenditure and ~20% decrements of intake. Research on the degree of increased activity or dietary changes that include energy reduction necessary for weight loss suggests that objective measurable differences can be undetectable, even if reported behavior varies between groups. At present, apart from body weight, objective measures of achievement of behavioral goals related to weight control is difficult.

To overcome the limitations of current methods to assess energy balance and control weight, innovative approaches are needed. The problems associated with measuring and monitoring components of human energy balance present unique opportunities for engineers with expertise in the disciplines of thermodynamics, mechanics, heat transfer, instrumentation, imaging, and design. By collaborating with obesity researchers, such engineers, especially those with biomedical backgrounds, may develop the novel approaches to successfully address the problem of obesity.

Each component of the energy balance equation presents unique challenges. For example, the difficulty of ascertaining food intake with acceptable levels of accuracy is well known to nutritionists. The standard self-report questionnaire

and recall techniques can provide valuable data on dietary patterns, and have been improved by electronic information technologies and by judicious use of results from cognitive process research. Nevertheless, these techniques are time-consuming and inconvenient. Furthermore, considerable under-reporting of total energy intake is typical, with this error more severe in overweight than non-overweight individuals. At the other extreme of precision and cost is the research technique (also occasionally used in therapeutic situations) of providing a controlled diet with all food intake observed and defined by chemical analysis. Use of these techniques is severely limited by their high cost and limited applicability because of the population samples typically enrolled and the highly controlled conditions used. Therefore, new and improved methods of determining energy intake are critically needed for research as well as practical purposes.

Measuring the various modes of physical activity is difficult as well, particularly outside the laboratory. Devices must be convenient, cost-effective, suitable for short-term and habitual activity, and valid for an array of circumstances and states of health and fitness. None of the available methods (pedometers, accelerometers, electronic load transducers, foot contact time monitors, heart rate monitoring) is fully satisfactory, because they only capture a fraction of needed information. They do not yield data that are easily understood, particularly by the lay public, nor can they easily detect changes in behavior, except for the pedometer, which yields data in terms of steps and can foster behavior change (i.e., more walking). In addition, the data yielded by these devices do not readily translate into calories expended over the entire course of a day, which must be compared with energy from food intake to obtain an estimate of energy balance. Therefore, there is a problem of inter-converting measurements of energy expenditure and intake into the same units as food intake.

Assessment of states of total energy balance also is a critical research need. Recently improved research tools include small or portable indirect calorimeters for short-term expenditure measurements during physical tasks, room calorimeters with floor mounted force plates to study movement energetics, and global positioning system (GPS) transponders to track outdoor activity patterns. Doubly-labeled water is valuable for determining total expenditure but is expensive, involves stable isotopes, and only is suitable for basic research. Nevertheless,

we need to be able to accurately, precisely, and directly measure whether an individual is in energy balance, deficit, or excess, and to translate the results into everyday behavior. The overall state of body energy stores also cannot be easily ascertained, particularly at the individual level, because data outputs are usually based on group-derived algorithms. However, there has been some recent progress in techniques used to estimate energy stores (e.g., bioelectric impedance for percent body fat, MRI-quantified adipose depots to define metabolically active compartments).

Such imaging and sensor technologies will also be beneficial to the elderly. In this population, such tools are needed to assess rates of change in total energy intake, balance, and expenditure, and in the size and function of multiple metabolic compartments (especially muscle mass), over relatively long intervals and in response to rare but cumulative events. These technologies need to be able to distinguish between changes related to the physiological process of aging, as opposed to age-associated ailments and other changes reflecting the health and social experience of the aged population. Any methodology used for the elderly population must accommodate a spectrum of functioning ranging from the unusually fit, to typical level, to the frail. Also, the information gathered should be translatable to research and/or practical applications related to preservation or impairment of ability to undertake activities of daily living. Assessment techniques and data analysis methods need to be able to distinguish between true capacity vs. elicited performance; these are highly variable among the aged, and are unusually susceptible to measurement biases and errors. Human factors issues are particularly important for the elderly population, and must acknowledge participant burdens related to time (including that of caregivers/assistants), transportation, cognitive capacity and effort, discomfort, and physical capabilities (such as vision, hearing, strength, mobility).

In conclusion, most techniques for measuring either side of the energy equation are costly, cumbersome, and suitable primarily for research use. They do not address the critical issue of overall energy balance, nor do they take advantage of new knowledge of biochemical markers. Moreover, the available devices are not sufficiently precise or specific for guiding individual behavior, and their

measurement errors may be greater than the treatment effect. Devices designed for use by the public are particularly hampered by these problems. At present, we do not have the equivalent of a "magic wristwatch" that can readily convey whether the wearer has exceeded an intake goal or fallen short on expenditure. New approaches might provide accurate, convenient, easily understood, and inexpensive devices to foster research and improve clinical management of adults and children.

The greatest scientific need is for improved ways to achieve short- and long-term measurement of total energy intake, expenditure, exchange, and balance, and components thereof (e.g., resting and basal metabolic rate, physical activity, thermic effect of food) under various physiologic conditions and activities, including work, sleep, and leisure activity, and related body composition and metabolic compartments. The use of micro-electro-mechanical systems for biomedical applications (BioMEMs) to measure appropriate biomarkers of energy balance may be of great benefit to assessing energy balance. Since many materials exhibit novel and unique properties at the nano level, their use might represent a new approach for precise measurements of energy status and metabolic activity.

#### Summary of priority areas

In summary, the objective of this PA is to encourage and enable engineers and scientists at small businesses to develop and evaluate new technologies, instrumentation, and medical devices to better assess appropriate biomedical parameters and provide feedback and/or therapy to reduce the prevalence of obesity and overweight. Development of new technologies and application of existing technologies may be proposed. Studies may include use of animal models and/or human participants, but are not required to do so. If appropriate, plans for manufacturing and clinical evaluation of developed instrumentation and medical devices should be included in the application.

Applications are encouraged that represent scientific and technical expertise and collaborations from fields such as biomedical engineering, computer sciences, physics, human and animal nutrition, aging, exercise sciences, behavioral sciences, medicine, biochemistry, and biotechnology.

Appropriate topics for development and validation under this PA include, but are not limited to, the following:

- o Diagnostic and therapeutic systems to monitor energy balance and appropriate biomarkers.

- o Biosensors, including intra- and extra-cellular systems, for measuring calorie consumption and energy expenditure. Sensors that are non-invasive, minimally invasive, miniature, stable, and durable.
- o Mathematical models for predicting interrelationships between energy balance and weight control.
- o Implantable devices for monitoring and treating obesity and overweight.
- o Bioengineering tools that integrate self-reported information with biologic and/or sensor measures of physical activity, diet/nutrition, and energy balance/obesity. This would include tools that measure this integrated information in real-time.
- o Methodologies for imaging structure and function, blood flow, perfusion, and metabolism from the molecular/cellular to whole organs for the purpose of measuring and studying energy balance, intake and expenditure, and weight control.
- o Miniaturized non-invasive sensors to detect motion, thermal output, pressure/other mechanical forces, body position, geophysical location;
- o Energy balance indicators, such as "smart" clothing, household or office furnishings, that incorporate sensors, bar codes or other identifying technologies to calculate energy expenditure.
- o Development of sensors to continuously measure physiological parameters/biomarkers which regulate or reflect appetite and metabolism (e.g. insulin, leptin, vagus nerve activity).

#### MECHANISM(S) OF SUPPORT

This PA uses the SBIR and STTR mechanisms, which are set-aside programs. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. Future unsolicited, competing-continuation applications based on this project will compete with all SBIR/STTR applications and will be reviewed according to the customary peer review procedures.

This PA uses just-in-time concepts. It also uses the modular budgeting format. Specifically, if you are submitting an application budget of \$100,000 total costs (direct, F&A and fee) or less, use the modular format and instructions as described in the current SBIR/STTR Omnibus Solicitation. Otherwise, follow the instructions for non-modular budget research grant applications. This program does not require cost sharing as defined in the current NIH Grants Policy

Statement at

[http://grants.nih.gov/grants/policy/nihgps\\_2003/NIHGPs\\_Part2.htm#matching\\_or\\_cost\\_sharing](http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPs_Part2.htm#matching_or_cost_sharing)

Applications may be submitted for support as Phase I STTR (R41) or Phase I SBIR (R43) grants, Phase II STTR (R42) or Phase II SBIR (R44) grants, or the SBIR/STTR FAST-TRACK option as described in the SBIR/STTR Omnibus Solicitation. Phase II applications in response to this PA will only be accepted as competing continuations of previously funded NIH Phase I SBIR/STTR awards. The Phase II application must be a logical extension of the Phase I research, but not necessarily a Phase I project supported in response to this PA.

#### PROJECT PERIOD AND AMOUNT OF AWARD

The SBIR/STTR Omnibus Solicitation indicates the statutory guidelines of funding support and project duration periods for SBIR and STTR Phase I and Phase II awards.

#### ELIGIBLE INSTITUTIONS

Eligibility requirements are described in the SBIR/STTR Omnibus Solicitation. Only small business concerns are eligible to submit applications. A small business concern is one that, on the date of award for both Phase I and Phase II agreements, meets ALL of the criteria as described in the SBIR/STTR Omnibus Solicitation.

#### INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs. On an SBIR application, the principal investigator must have his/her primary employment (more than 50%) with the small business at the time of award and for the duration of the project. The PI on an STTR application may be employed with the small business concern or the participating non-profit research institution as long as she/he has a formal appointment with or commitment to the applicant small business concern, which is characterized by an official relationship between the small business concern and that individual.

#### SPECIAL REQUIREMENTS

##### Grantees' Meetings

In order to ensure maximum progress in the projects funded by this PA and to

realize the maximum benefit for the research community, all funded investigators will be invited to an annual meeting of investigators funded by SBIR/STTR. The annual meeting will facilitate sharing of progress and research insights with other investigators. In the preparation of the budget, applicants should request travel funds for the Principal Investigator and one additional senior investigator to attend this annual meeting.

#### WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into two areas:

scientific/research and financial or grants management issues:

o Direct your questions about scientific/research issues to:

#### NHLBI

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NIA

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o Direct your questions about financial or grants management matters to:

Mr. Edward (Gene) McGeehan  
Grants Operations Branch  
Division of Extramural Affairs  
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6701 Rockledge Drive, MSC 7926  
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FAX: (301) 480-0422  
Email: [mcgeehae@nhlbi.nih.gov](mailto:mcgeehae@nhlbi.nih.gov)

#### SUBMITTING AN APPLICATION

The PHS 398 research grant application must be used for all SBIR/STTR Phase I, Phase II and Fast-Track applications (new and revised.) Effective October 1, 2003, applications must have a DUN and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for federal grants or cooperative agreements. The DUNS number can be obtained by calling (866) 705-5711 or through the web site at <http://www.dunandbradstreet.com/>. The DUNS number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html>. Prepare your application in accordance with the SBIR/STTR Omnibus Solicitation and the PHS 398. Helpful information for advice and preparation of the application can be obtained at: <http://grants.nih.gov/grants/funding/sbirgrantsmanship.pdf>. The NIH will return applications that are not submitted on the 5/2001 version of the PHS 398. For further assistance contact GrantsInfo, Telephone: (301) 435-0714, Email: [GrantsInfo@nih.gov](mailto:GrantsInfo@nih.gov).

The title and number of this PA must be typed on line 2 of the face page of the application.

#### SUPPLEMENTARY INSTRUCTIONS

Certain types of research require clinical evaluation and federal regulatory approvals prior to commercialization. Applicants are encouraged to contact the FDA to identify approvals which may be required in the course of development and to obtain guidance regarding data required by the FDA to obtain such approvals. Applicants may include FDA guidance in the application to justify experimental

plan.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review  
National Institutes of Health  
6701 Rockledge Drive, Room 1040, MSC 7710  
Bethesda, MD 20892-7710 Bethesda, MD 20817 (FOR EXPRESS/COURIER SERVICE)

APPLICATION PROCESSING: Applications must be mailed on or before the receipt dates described on the first page of this program announcement. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an unfunded version of an application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight weeks.

#### PEER REVIEW PROCESS

Applications submitted for this PA that are complete will be assigned on the basis of established PHS referral guidelines. Appropriate scientific review groups convened in accordance with the standard NIH peer-review procedures (<http://www.csr.nih.gov/refrev.htm>) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
- o Receive a written critique
- o Receive a second level review by the appropriate national advisory council or board

#### REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological

systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have

a substantial impact on the pursuit of these goals:

- o Significance
- o Approach
- o Innovation
- o Investigator
- o Environment

#### ALL SBIR/STTR APPLICATIONS

1. Significance: Does the proposed project have commercial potential to lead to a marketable product or process? Does this study address an important problem? What

may be the anticipated commercial and societal benefits of the proposed activity?

If the aims of the application are achieved, how will scientific knowledge be advanced? Does the proposal lead to enabling technologies (e.g., instrumentation, software) for further discoveries? Will the technology have a competitive advantage over existing/alternate technologies that can meet the market needs?

2. Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project?

Is the proposed plan a sound approach for establishing technical and commercial

feasibility? Does the applicant acknowledge potential problem areas and consider

alternative strategies? Are the milestones and evaluation procedures appropriate?

3. Innovation: Does the project challenge existing paradigms or employ novel technologies, approaches or methodologies? Are the aims original and innovative?

4. Investigators: Is the Principal Investigator capable of coordinating and managing the proposed SBIR/STTR? Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers, including

consultants and subcontractors (if any)? Are the relationships of the key personnel to the small business and to other institutions appropriate for the work proposed?

5. Environment: Is there sufficient access to resources (e.g., equipment, facilities)? Does the scientific and technological environment in which the work

will be done contribute to the probability of success? Do the proposed experiments

take advantage of unique features of the scientific environment or employ useful

collaborative arrangements?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, the following items will be applied to ALL applications in the determination of scientific merit and the priority score:

PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. (See additional information and criteria included in the section on Federal Citations, below.)  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

INCLUSION OF WOMEN, MINORITIES AND CHILDREN IN RESEARCH: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See additional information and Inclusion Criteria in the sections on Federal Citations, below.)

Human Subjects:

1. Protection of Human Subjects from Research Risks - for all studies involving human subjects. See instructions and "Guidance for Preparing the Human Subjects Research Section." If an exemption is claimed, is it appropriate for the work proposed? If no exemption is claimed, are the applicant's responses to the six required points appropriate? Are human subjects placed at risk by the proposed study? If so, are the risks reasonable in relation to the anticipated benefits to the subjects and others? Are the risks reasonable in relation to the importance of the knowledge that reasonably may be expected to be gained? Are the plans proposed for the protection of human subjects adequate?

2. Inclusion of Women Plan - for clinical research only. Does the applicant propose a plan for the inclusion of both genders that will provide their appropriate representation? Does the applicant provide appropriate justification when representation is limited or absent? Does the applicant propose appropriate and acceptable plans for recruitment/outreach and retention of study participants?

3. Inclusion of Minorities Plan - for clinical research only. Does the applicant

propose a plan for the inclusion of minorities that will provide their appropriate representation? Does the applicant provide appropriate justification when representation is limited or absent? Does the applicant propose appropriate and acceptable plans for recruitment/outreach and retention of study participants?

4. Inclusion of Children Plan- for all studies involving human subjects. Does the applicant describe an acceptable plan in which the representation of children of all ages (under the age of 21) is scientifically appropriate and recruitment/retention is addressed realistically? If not, does the applicant provide an appropriate justification for their exclusion?

5. Data and Safety Monitoring Plan - for clinical trials only. Does the applicant describe a Data and Safety Monitoring Plan that defines the general structure of the monitoring entity and mechanisms for reporting Adverse Events to the NIH and the IRB?

CARE AND USE OF VERTEBRATE ANIMALS IN RESEARCH: If vertebrate animals are to be used in the project, the required five items described under Vertebrate Animals (section f of the Research Plan instructions) will be assessed.

BIOHAZARDS: Is the use of materials or procedures that are potentially hazardous to research personnel and/or the environment proposed? Is the proposed protection adequate?

ADDITIONAL REVIEW CONSIDERATIONS: The following items may be also be considered by reviewers but will not be included in the determination of scientific merit.

SHARING RESEARCH DATA: Applicants requesting \$500,000 or more in direct costs in any year of the proposed research must include a data sharing plan in their application. The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or priority score.

BUDGET: The reasonableness of the proposed budget may be considered. For all applications, is the percent effort listed for the PI appropriate for the work proposed? On applications requesting up to \$100,000 total costs, is the overall budget realistic and justified in terms of the aims and methods proposed?

On applications requesting over \$100,000 in total costs, is each budget category realistic and justified in terms of the aims and methods?

PERIOD OF SUPPORT: The appropriateness of the requested period of support in relation to the proposed research.

#### PHASE II APPLICATIONS

In addition to the above review criteria:

1. How well did the applicant demonstrate progress toward meeting the Phase I objectives, demonstrating feasibility, and providing a solid foundation for the proposed Phase II activity?
2. Did the applicant submit a concise Commercialization Plan that adequately addresses the seven areas described in the Research Plan item J?
3. Does the project carry a high degree of commercial potential, as described in the Commercialization Plan?

#### AMENDED APPLICATIONS

In addition to the above criteria, the following criteria will be applied to revised applications.

1. Are the responses to comments from the previous SRG review adequate?
2. Are the improvements in the revised application appropriate?

#### PHASE I/PHASE II FAST-TRACK APPLICATION REVIEW CRITERIA

For Phase I/Phase II Fast Track applications, the following criteria also will be applied:

1. Does the Phase I application specify clear, appropriate, measurable goals (milestones) that should be achieved prior to initiating Phase II?
2. Did the applicant submit a concise Commercialization Plan that adequately addresses the seven areas described in the Research Plan, item J?
3. To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?
4. Does the project carry a high degree of commercial potential, as described in the Commercialization Plan?

Phase I and Phase II Fast-Track applications that satisfy all of the review criteria will receive a single rating. Failure to provide clear, measurable goals may be sufficient reason for the scientific review group to exclude the Phase II application from Fast-Track review.

#### AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended SBIR and STTR applications. The following will be considered in making funding decisions:

- o Scientific merit of the proposed project as determined by peer review
- o Availability of funds
- o Relevance to program priorities

For FAST-TRACK applications, the Phase II portion may not be funded until a Phase

I final report and other documents necessary for continuation have been received and assessed by program staff that the Phase I milestones have been successfully achieved.

#### RECEIPT AND REVIEW SCHEDULE

See [http://grants1.nih.gov/grants/funding/sbirsttr\\_receipt\\_dates.htm](http://grants1.nih.gov/grants/funding/sbirsttr_receipt_dates.htm)

#### REQUIRED FEDERAL CITATIONS

ANIMAL WELFARE PROTECTION: Recipients of PHS support for activities involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of

Laboratory Animals

(<http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf>), as mandated by the Health Research Extension Act of 1985

(<http://grants.nih.gov/grants/olaw/references/hreal985.htm>), and the USDA Animal

Welfare Regulations (<http://www.nal.usda.gov/awic/legislat/usdaleg1.htm>), as applicable.

HUMAN SUBJECTS PROTECTION: Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the

risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance

of the knowledge gained or to be gained.

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

DATA AND SAFETY MONITORING PLAN: Data and safety monitoring is required for all

types of clinical trials, including physiologic, toxicity, and dose-finding studies (phase I); efficacy studies (phase II); efficacy, effectiveness and comparative trials (phase III). The establishment of data and safety monitoring

boards (DSMBs) is required for multi-site clinical trials involving interventions

that entail potential risk to the participants. (NIH Policy for Data and Safety

Monitoring, NIH Guide for Grants and Contracts, June 12, 1998:

<http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

SHARING RESEARCH DATA: Starting with the October 1, 2003 receipt date, investigators submitting an NIH application seeking \$500,000 or more in direct

costs in any single year are expected to include a plan for data sharing or state why this is not possible. [http://grants.nih.gov/grants/policy/data\\_sharing](http://grants.nih.gov/grants/policy/data_sharing) Investigators should seek guidance from their institutions, on issues related to institutional policies, local IRB rules, as well as local, state and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a complete copy of the updated Guidelines are available at [http://grants.nih.gov/grants/funding/women\\_min/guidelines\\_amended\\_10\\_2001.htm](http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm)

The amended policy incorporates: the use of an NIH definition of clinical research, updated racial and ethnic categories in compliance with the new OMB standards, clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398, and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS: The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH,

unless there are scientific and ethical reasons not to include them. The inclusion of children is not necessary if the proposed research is focused on the aged population.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at <http://grants.nih.gov/grants/funding/children/children.htm>.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with federal funds and (2) cited publicly and officially by a federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at [http://grants.nih.gov/grants/policy/a110/a110\\_guidance\\_dec1999.htm](http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm).

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

STANDARDS FOR PRIVACY OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION: The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information," the "Privacy Rule," on August 14, 2002. The Privacy Rule is a federal regulation

under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (<http://www.hhs.gov/ocr/>) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html>.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review, because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at <http://www.cfda.gov/> and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm>

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.