SECTION C – DESCRIPTION/SPECIFICATION/WORK STATEMENT

ARTICLE C.1. BACKGROUND

Functional neuromuscular stimulation (FNS) has been successfully applied to assist tetraplegic individuals in the partial restoration of hand and arm movements. FNS applications, such as Freehand, have been developed that electrically stimulate the nerves associated with paralyzed muscle groups in the hand and arm to restore some functional hand grasp to persons with spinal cord injuries at C5 or C6. FNS options available to individuals with other levels of cervical injury have been limited, however, it is clear that complex control needed to restore functional movement across two or more joints to persons with higher cervical injuries can be generated through the coordinated stimulation of multiple nerves coupled with sensory feedback. Significant progress has been made recently in the development of enabling technology and understanding that will lead to the expansion of FNS to a wider range of individuals living with cervical injuries. These recent developments include multi-contact cuff electrode technologies, comprehensive models of muscle activation patterns underlying arm and hand movements, the refinement of surgical/monitoring protocols, and multi-channel feedback control stimulators. In addition, significant progress has been made in utilizing peripheral control signals, such as those based on electromyography, which could be used to derive the intent of movement. There have been exciting recent developments in fields of brain-machine interfaces (BMIs) and brain-computer interfaces (BCIs) where it is conceivable to eventually be able to extract high level control information to guide upper limb movement. While the National Institute of Neurological Disorders and Stroke (NINDS) supports the development of BMI and BCI systems, these systems are at an early stage of development such that it is presently unclear what specifications these systems must meet to provide sufficiently robust and reliable control signals for upper limb control.

This project involves research and development leading to the complete development of systems for FNS devices designed for subjects with high, middle, and low cervical injuries. This project will focus on the sufficiency of FNS in the restoration of coordinated upper extremity function movements such as hand grasp, pronation/supination, elbow extension and shoulder movement. To make the systems practical and attractive for use, the FNS system components will need to be made fully implantable, including sensors that provide the system and/or the user with sensory feedback and a paradigm for control. The contractor shall establish safety and feasibility of the proposed approach, the ability of the FNS system to synergistically control stimulated and voluntary movements, determine the most effective sensory and control components, and determine the quantitative metrics needed for testing system efficacy in restoration of upper extremity movements in human subjects. Spinal cord injury induces changes in muscle properties that vary between individuals based on the extent of denervation and disuse. Therefore, the following issues should be addressed: assessment of spasticity and the effects of muscle denervation, weakness, fatiguability and/or other complications on FNS system performance. While this contract does not constitute a clinical trial, it is expected that a sufficient number of human subjects will be enrolled in the study to enable statistical confidence in the findings, and establish appropriate

inclusion/exclusion criteria and endpoints for planning definitive efficacy trials. A major goal of this effort is to enable transition to the commercial sector of technologies that can benefit disabled individuals. Consequently, a successful proposal will include a commercial transition plan for relevant milestones, deliverables, and accomplishments resulting from this effort.

The contractor will also cooperate with other investigators supported by the Neural Prosthesis Program (NPP) largely driven by the National Institute of Neurological Disorders and Stroke as well as other institutes at the NIH. Of particular relevance to this RFP, The National Institute of Child Health and Human Development (NICHD) is planning to support an effort to fabricate a prototype FNS controller capable of translating motor cortical signals to signals necessary to drive a FNS system. The contractor for this RFP will be expected to collaborate with the selected NICHD performers. This RFP represents a competitive renewal of a contract that will expire in November 2005.

ARTICLE C.2. STATEMENT OF WORK

Independently, and not as an agent of the Government, the contractor shall develop FNS systems to restore coordinated, directed upper extremity function by synergistically controlling stimulated and voluntary movements in tetraplegic individuals with high, middle, and low cervical injuries. Evaluation of these FNS systems will be conducted in human subjects who have paralyzed upper extremities as a result of upper motor neuron lesions. A major emphasis of this work is to produce functionally relevant quantitative measures; any testing performed should primarily emphasize quantitative results rather than qualitative or descriptive research findings.

Specifically, the contractor shall:

1. Identify and justify the choice of technologies that can be effectively developed to restore functional movements to targeted populations of individuals with high, middle and low cervical injuries. The Contractor shall define criteria to select candidates for testing of FNS systems based upon the level of their injury, completeness, specific functional measures, or other relevant criteria. Whenever possible, the subject populations should include women and minorities.

2. Design, implement, and test fully implantable FNS systems to restore movements such as hand grasp, pronation/supination, elbow extension and/or shoulder movement to allow purposeful movements to individuals with tetraplegia. It is expected that the resulting systems will be capable of sophisticated combinations of upper extremity movements that enable functionally relevant actions appropriate for individuals with mid- and high-level spinal cord injury. The contractor shall provide a comprehensive description of the functional and purposeful movements that will be enabled by the implanted system and a rationale addressing why this function is important to individuals with a particular

class of spinal cord injury. Quantitative performance and reliability specifications for the components of the implantable system will be fully documented by the contractor.

3. By the end of the second year of the project, begin studies characterizing the performance of the implanted FNS systems in human subjects using quantitative metrics, where an appropriate number of subjects shall be evaluated to enable statistical significance. It is expected that these metrics will be readily applicable for future efficacy testing in clinical trials and be defined through consultation with the NINDS Program Officer.

4. Assess, for periods of at least six months after implantation, strength of voluntary and stimulated movements, spasticity, and fatigue characteristics, as well as addressing any physiologic complications and safety concerns arising in the individuals with fully implantable FNS systems.

5. Develop a means to relate the performance of the system(s) under development to the effects of muscle denervation, disuse atrophy and/or strengthening due to FNS. The contractor shall then characterize the effects of muscle denervation, fatigue, and spasticity on FNS system performance.

6. Using a quantitative model, the contractor shall systematically evaluate the BMI/BCI systems for capacity to provide control signals reflecting volitional control of movement. Develop a simulation tool that will enable a variety of BMI and BCI approaches to be evaluated for suitability as command signal sources to drive implanted neural prostheses for high level tetraplegia. The simulation tool shall be capable of real time simulation of upper extremity musculoskeletal activation in response to various high level control paradigms. The simulation tool shall allow the user to restrict the group of muscles available for stimulation to mimic denervation conditions associated with spinal cord injury. The contractor shall provide for the dissemination of the simulation tool to the Neural Prosthesis community. The contractor shall establish scientific contact with the BMI and BCI communities for intellectual exchange through the duration of the contract.

7. Within the first 30 days of the base contract period, submit a protocol to the local Institutional Review Board to cover the initial screening of potential candidates for the neuroprostheses under development in this contract. Once approved by the local IRB (but within the first 90 days of the contract), the contractor shall submit this screening protocol for evaluation and approval to the Project Officer. Specifically, the following human subjects related documentation shall be submitted: protocol for the local institution, consent form, NINDS Human Subjects Clearance Form, and any other needed documentation. Documentation for all other protocols shall be submitted by no later than the end of the second year of the contract period.

8. Provide a comprehensive transition plan where the technology, milestones, and/or accomplishments developed under this effort will reach the commercial sector.

9. Cooperate with other investigators in the Neural Prosthesis Program by collaboration and sharing of experimental findings. In particular, the contractor shall share system interface specifications with the designated performer of the NICHD sponsored FNS controller project to ensure compatibility.

10. Through consultation with the NINDS Clinical Trials cluster, or appropriate contacts as identified by the NINDS Project Officer, and FDA contacts, draft a plan for a clinical trial to demonstrate efficacy of one or more of the implanted systems.

ARTICLE C.3. TECHNICAL REPORTING REQUIREMENTS

In addition to those reports required by the other terms of this contract, the Contractor shall prepare and deliver the following reports in the manner stated below during the base, and if exercised, the option periods in accordance with ARTICLE F.2. DELIVERIES of this contract:

1. **Quarterly Technical Progress Reports:** These reports shall be submitted electronically as Adobe PDF or Microsoft Word documents to both the Contracting Officer and Project Officer, the reports are due 10 days after the end of the reporting period. The e-mail delivery addresses for both the Contracting Officer and the Project Officer are specified in ARTICLE F.2. DELIVERIES of this contract. These reports shall be in the following format:

    a. Executive Summary – brief description of the overall goals of the contract and the major contents of the current quarterly report (no more than 1 page).
    b. Activity Summary – bullets summarizing major positive or negative results, meetings, presentations, publications and patents related to the contract during the reporting period (no more than 1 page).
    c. Research Results and Discussion – for each experiment and set of observations, a brief statement of rationale followed by description of experimental results with sufficient detail to permit adequate interpretation. Following a short discussion/interpretation of results, future plans for the next two reporting periods should be identified (no more than 10 pages).
    d. Concerns – identify any issues where NINDS program involvement may be required or helpful. For deviations from the schedule for deliverables, the underlying cause(s), and potential solutions should be listed. In addition, any changes in personnel that impact to the progress of the contract should be identified (no more than 2 pages).

2. **Base Contract Period Final Report:** Prepare and deliver a report, no later than 60 days prior to the end of the base contract period, detailing performance on at least the tasks delineated for the base period performance. This report shall be

submitted electronically as Adobe PDF or Microsoft Word documents to both the Contracting Officer and Project Officer. The Project Officer shall review the draft report and provide the Contracting Officer with comments within 7 work days after receipt. The final report shall be corrected by the contractor, if necessary, and the final version delivered in accordance with Section F, Deliveries or Performance, of the contract. The base contract final report shall summarize what was achieved, what was not achieved, and a detailed timeline for the achievement of the remaining tasks. This report may refer to quarterly reports and published articles supported by the contract. Copies of all publications, but not quarterly progress reports, shall be included in the base contract final report. Any substantive data or other results obtained during the final quarter should be included as an addendum.

3. **Option Period Final Report**: If the option period is exercised, the contractor shall prepare and deliver a draft comprehensive report, 14 working days before the termination and/or completion date of the contract, detailing performance on all of the contract tasks during the option period . This draft report shall be submitted electronically as Adobe PDF or Microsoft Word documents to both the Contracting Officer and Project Officer. The Project Officer shall review the draft report and provide the Contracting Officer with comments within 7 working days after receipt. The final report shall be corrected by the contractor, if necessary, and the final version delivered by the termination and/or completion date of the contract. The option period final report shall summarize what was achieved, what was not achieved, and shall include recommendations for future research and development in the area. This report may refer to quarterly reports and published articles supported by the contract. PDFs of all publications, but not quarterly progress reports, shall be included with the submission of the option contract final report. Any substantive data or other results obtained during the final quarter should be included as an addendum.

ARTICLE C.4. SPECIAL REQUIREMENTS

The contractor shall attend and offer a presentation at the annual NIH Neural Prosthesis Workshop as determined by the NINDS Project Officer.

ARTICLE C.5. STRUCTURE OF THE CONTRACT

1. **The Base Contract Period** shall consist of a 30-month performance period. During the base contract period the Contractor shall, at a minimum:
    a. Complete work on items 1, 7, and 8 listed above in section C.2.
    b. Attend and participate in the annual workshop to interact with other members of the Neural Prosthetics community.
    c. Provide a comprehensive description of the functional and purposeful movements that will be enabled by the implanted systems for targeted populations of individuals with high, middle, and low cervical injuries.

d. Subject to prior approval of the selected BMI systems by the Project Officer, provide a quantitative assessment of the capacity of two BMI systems to generate suitable control signals for FNS systems using computational simulation system.
e. Develop a means to relate the performance of the system(s) under development to the effects of muscle denervation, disuse atrophy and/or strengthening due to FNS.
f. Prepare and deliver to the NINDS Project Officer and NINDS Contracting Officer a base contract final report.

It is the intent of the Government to encourage the collection of supplementary data, beyond that which is minimally required above for the base period, which supports the likely success for meeting and exceeding the overall goal of this effort. Potential supplementary data must pertain to the tasks identified in section C.2, which have not been required for completion during the base contract period.

2. **Option Period**: Based on the Contractor's performance during the base contract period, the Government may unilaterally extend the period of this contract for an option period of 30 months. The desired milestones and deliverables for the base contract period are outlined above and the final option period must demonstrate completion of all remaining tasks listed in section B of the Statement of Work. The Contractor is expected to provide a comprehensive and coherent timeline for deliverables, milestones, and accomplishments for lifetime of the project. Exercise of the future option will be contingent upon: 1) the level and degree of performance by the Contractor in meeting deliverables, milestones, and accomplishments according to the timeline; 2) Government's continuing need for development of the system; 3) quality of data generated and any other supplementary data; and 4) availability of funds.

ARTICLE C.6. INVENTION REPORTING REQUIREMENT

All reports and documentation required by FAR CLAUSE 52.227-11, including, but not limited to, the invention disclosure report, the confirmatory license, and the government support certification, shall be directed to the Office of Extramural Inventions and Technology Resources Branch, OPERA, NIH, 6705 Rockledge Drive, Room 1040 A, MSC 7980, Bethesda, Maryland 20892-7980 (Telephone: 301/435-1986). In addition, one copy of the annual utilization report and a copy of the final invention statement, shall be submitted to the Contracting Officer at the address listed below. The final invention statement (see FAR 27.303(a)(2)(ii)) shall be submitted within 90 days after contract expiration to the following address:

Contracting Officer
National Institutes of Health
National Institute of Neurological Disorders and Stroke
6001 Executive Boulevard, Suite 3287, MSC 9531
Bethesda, MD 20892-9531

To assist contractors in complying with invention reporting requirements of the clause, the NIH has developed "Interagency Edison," an electronic invention reporting system. Use of Interagency Edison is encouraged as it streamlines the reporting process and greatly reduces paperwork. Access to the system is through a secure interactive Web site to ensure that all information submitted is protected. Interagency Edison and information relating to the capabilities of the system can be obtained from the Web (http://www.iedison.gov), or by contacting the Office of Extramural Inventions and Technology Resources Branch, OPERA, NIH.