SECTION C -- DESCRIPTION/SPECIFICATION/WORK STATEMENT

ARTICLE C.1. STATEMENT OF WORK

a. **Background**:

Recently, the Repair and Plasticity (RP) cluster of the National Institute of Neurological Disorders and Stroke (NINDS) initiated a research program to study spinal cord circuitry, plasticity in spinal cord circuits and spinal interneurons (http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-99-008.html). The research supported through this initiative as well as ongoing research on the neurobiology of the spinal cord and spinal cord injury will advance our understanding of the function and dysfunction of the spinal cord. Also recent investigations have demonstrated that microelectrodes can be safely implanted into the spinal cord and that stable microstimulation of small neural populations can be accomplished over periods of months (Exp Neurol. 2000;163:422-9). It is still to be demonstrated that our increased understanding of the function of the spinal cord combined with an ability to selectively microstimulate select neural populations can lead to significant functional improvement in spinal cord injured individuals.

The Neural Prosthesis Program (NPP) in the RP cluster supports the development of neural prostheses to restore lost function in neurologically injured individuals. Neural prostheses replace or supplement neurological function by directly interfacing with the nervous system. Microstimulation with microelectrodes implanted into neural tissue in the spinal cord can directly activate neural circuits. Microstimulation may also functionally modify the neural circuitry in the spinal cord. Animal and human studies have shown the potential of microstimulation to provide focal, controlled activation of neural tissue. At the same time, studies of spinal cord circuitry have demonstrated plastic circuitry that might be functionally activated and or modified by suitable microstimulation with or without other sensory stimulation.

Efforts have been initiated to explore the possible use of chronic microstimulation of the spinal cord to restore motor function. If successful, such a technique could be part of a prosthesis to restore genito-urinary, bowel, and other motor functions to victims of spinal cord injury. In particular, evidence from current studies indicate that is possible to selectively excite neurons innervating the bladder detrusor muscle while simultaneously stimulating interneurons which have inhibitory synaptic connections with neurons innervating the external urethral sphincter. Likewise, discrete control of penile erection, ejaculation and bowel evacuation may be possible by selective spinal cord microstimulation below the level of spinal cord injury.

Current research has provided information about the locations of afferent and efferent neurons as well as interneurons controlling urinary function in the cat spinal cord using both normal and acutely spinalized animals. Studies have demonstrated the possibility of activating bowel and genito-urinary function in intact animals and in acutely spinalized animals.(IEEE Trans Rehab Eng. 1998, 6:374-81, Brain Res.

1999;836:19-30). Now studies are needed to demonstrate the feasibility of functional restoration in chronically spinalized animals.

b. **Technical Specifications**:

Independently, and not as an agent of the Government, the Contractor shall design, develop, and evaluate microstimulation of the lumbosacral spinal cord as a method of controlling genito-urinary and bowel function. Male and female animal models should be investigated for studies of bladder and bowel function.

Specifically, the Contractor shall:

1. Select a non-human, animal model, excluding chimpanzees, of complete thoracic spinal cord injury taking into consideration factors that shall include:

   (a) similarities and differences of the animal model and human motor systems innervated by lumbosacral motor neurons.
   (b) similarities and differences of the genito-urinary and bowel, systems in chronic spinal cord lesioned animals to humans with spinal cord injuries.
   (c) the size and mobility of the spinal cord within the vertebral canal.
   (d) the suitability for tolerating a chronic, complete, spinal cord lesion and resulting lower body paralysis.

2. Develop or obtain the following technology:

   (a) Surgical techniques, microelectrodes and associated cables and percutaneous connectors to permit multiple microelectrodes to be chronically placed in the lumbar and sacral spinal cord of spinal injured animals. Techniques shall support the placement of at least six microelectrodes for periods of at least ten months.
   (b) Surgical methods to optimally place microelectrodes into target areas for functional microstimulation in the areas expected to effect genito-urinary and bowel function.
   (c) Methods to record from the microelectrodes when they are not being used for stimulation.
   (d) A pressure monitoring system for use in the animal model capable of acutely measuring pressures within the distal urethra, within the urethral sphincteric region, within the bladder, across the bladder wall, within the colon, and within the anal sphincter region while the animal is anesthetized. The system shall also be capable of recording urine flow in non-anesthetized animals.

3. In chronic spinal cord transected animals, with arrays of six or more microelectrodes whose exposed surface areas are equal to or less than 1000 square

microns, determine the effectiveness and selectivity of microstimulation of the target neuronal populations in producing:

(a) detrusor contraction.
(b) urinary sphincter inhibition.
(c) evacuation of bladder contents.
(d) penile erections.
(e) ejaculation.
(f) coordinated colonic contractions.
(g) anal sphincter inhibition.

4. In chronic spinal cord transected animals, using arrays of six or more microelectrodes whose exposed surface areas are equal to or less than 1000 square microns, investigate the effects microstimulation in association with sensory stimulation or other physical therapy and/or focal pharmacological intervention on sensory triggered:

   (a) detrusor contraction.
   (b) urinary sphincter inhibition.
   (c) evacuation of bladder contents.
   (d) penile erections.
   (e) ejaculation.
   (f) coordinated colonic contractions.
   (g) anal sphincter inhibition.

5. In the same animals used for microstimulation, attempt to develop a method of electrically mapping the surface of the lumbosacral spinal cord with a surface stimulating electrode to determine the approximate location of the neuronal populations mapped in 3. above to a degree of accuracy which would be useful in future human spinal cord implants where microscopic anatomical maps are not available.

6. Based on the results of these studies prepare a plan for further feasibility studies of genito-urinary prostheses and bowel prosthesis for paralyzed humans.

7. Upon completion of the tasks specified above prepare and deliver to the government a comprehensive final report that shall summarize what was achieved, what was not achieved, and shall include recommendations for future research and development in this research area.