SECTION C -- DESCRIPTION/SPECIFICATION/WORK STATEMENT

ARTICLE C.1. BACKGROUND

Packaging is a critical issue in all implantable biomedical applications and particularly for implanted neural prostheses. Yet despite its importance, a hermetic package in the form of a metal, ceramic or glass can has been and remains essentially the only means available for packaging implanted electronic devices for long-term human applications. While the hermetic can has served well in the pacemaker industry, the requirements for increased numbers of electrodes and increased miniaturation leads to the requirement for new packaging methods for microsize neural implants. The central nervous system (CNS) presents a special environment for implants. Devices and insulating biomaterials placed here benefit from the mechanical protection that is afforded to CNS tissue by the skull and spinal canal. However, the extracellular fluid (ECF) environment is also a harsh one for microelectronic devices and microwires and cables. Ions from the salts in the ECF as well as a variety of proteins and lipids can degrade or change the properties of an insulating coating. Insulating biomaterials intended for implants into the central nervous system need to protect devices from this hostile ionic environment of extracellular fluids for the lifetime of an implant recipient. In the case of materials used for devices implanted in young children, this might extend to 100 years.

Studies in the Neural Prosthesis Program have demonstrated reliable operation in *in-vitro* soak tests of polymer insulated silicon chips and wires for periods of over ten years. Accelerated life testing of these same materials suggests that they will function reliably for a lifetime as required. These promising results must be balanced with the observation that the results have been difficult to transfer to other investigators because of stringent requirements for properly cleaned substrates. Also, major failures such as lead wire fracture following encapsulation in connective tissue and breakdown of insulation on pacemaker lead wires were discovered in *in vivo* studies or clinical applications. *In-vivo* evaluation in a good model of the target application remains the gold standard for evaluation of insulating biomaterials. However, it is not realistic to test materials in this setting for 100 years. Some methods are needed to accelerate the test.

The polymers that have been successful in *in-vitro* tests are in the classes of the fluropolymers and silicones. Silicones are particularly promising as insulating materials because they both insulate wires and insulate the surface of implanted silicon microelectrode arrays by chemical bonding. Fluropolymers have so far failed to adhere to silicon microdevices during saline soak testing. A new class of materials, liquid-crystal polymers, also appears promising in pilot studies. These materials may be particularly valuable for use in electronic implants because they are dimensionally stable permitting them to be patterned with conductive leads.

In-vivo studies of the silicone, fluropolymer, and liquid-crystal insulating materials are essential. In order to estimate the long-term, *in-vivo* survival of insulating systems in reasonable time periods it is desirable to develop and validate an accelerated *in-vivo* testing system. It is not possible to increase temperature to accelerate *in-vivo* tests but it is feasible to use a combination of more sensitive measurements and other accelerators to

detect early signs of decreased performance that may be predictive of failure. This research and development work will develop an implantable test system to evaluate the long-term stability of insulating biomaterials. Consideration will be given to increasing electrical stress, increasing sensitivity of measurements, increasing sensitivity of test devices, and increasing mechanical stress as means to accelerate the *in-vivo* testing of insulating biomaterials. In addition, ongoing *in-vitro* testing of promising materials will continue.

ARTICLE C.2. STATEMENT OF WORK

Independently, and not as an agent of the Government, the contractor shall develop and evaluate insulating biomaterials that function reliably over the lifetime of an implant recipient. Testing of these materials shall be done both *in-vitro* (under physiologic and accelerated test conditions) and *in-vivo*. These biomaterials shall be suitable for insulating silicon-based, micromachined microelectrode arrays and connecting wire microcables that are placed in the central nervous system. The contractor shall develop and validate evaluation methods to test the long-term survival and biocompatibility of implanted devices protected using the developed insulating biomaterials.

Specifically, the Contractor shall:

a. Conduct *in-vitro* testing of new insulating biomaterials materials as they become available and continue testing fluorocarbon, silicone and LCP polymers presently under test. At the beginning of the contract the Project Officer will deliver to the contractor up to 300 microwires and microdevices presently under soak testing in 0.9% saline.

    1. Insulated conductors shall be tested at potentials of plus and minus 5 volts with respect to a 0.9% saline soak bath. Samples shall be maintained at 37 degrees C. (or for devices under accelerated testing at 90 degrees C.) for the duration of the contract or until they fail. Leakage current from the conductor to the bath shall be monitored at least monthly.

    2. If insulators fail, as indicated by DC leakage currents of greater than 5 picoampres, the failure mechanism(s) of the insulators shall be determined and this information shall be used to improve the insulation system and to select new insulators if appropriate.

    3. Insulated microassemblies consisting of a cable of at least 2 microwires terminated on a silicon micromachined structure shall also be used for evaluating the insulating materials. Design rules for the silicon microstructures shall follow those defined by the University of Michigan Center for Neural Communication Technology. (Design rules and a description of available microelectrodes can be found at www.engin.umich.edu/center/cnct).

b. Accelerated *in-vitro* testing shall be used to identify insulating materials expected to function for a lifetime under normal physiological conditions.

c. The Contractor shall investigate the factors related to material preparation and coating deposition, such as surface preparation, that are associated with successful and unsuccessful insulating coatings of the most promising insulating materials. The contractor shall develop protocols for material preparation and deposition based on these studies that will lead to reproducible, reliable insulation of implanted devices and wires.

d. The contractor shall develop an *in-vivo* test system for testing insulating biomaterials implanted in the central nervous system.

    1. The test system shall be designed to permit testing of microdevices for periods exceeding 20 years.

    2. The test system shall be capable of measuring DC leakage currents in the picoamp range in implanted microwires.

    3. The test system shall permit daily recording of leakage current through insulation as well as measuring critical device parameters of implanted solid state and thin-film components integrated into micro electronic devices.

    4. The test system shall permit in-vivo testing of the microcables, microelectrodes, and microassemblies described in section a.

e. The contractor shall design an *in-vivo* test system for accelerated testing of biomaterials implanted in the CNS that shall be capable of testing components as described in section d. Consideration shall be given to developing a validation procedure for the acceleration rate(s) of the accelerated test system.

f. Insulating biomaterials that by *in-vitro* testing appear functional shall be tested *in-vivo* using the test system developed in section d.

    1. Select a suitable animal model (excluding chimpanzees) for implantation of microcables and microdevices. The test devices shall be implanted within the central nervous system.

    2. Monitor leakage currents at least weekly for periods of at least 2 years.

        a) If insulators fail to maintain their insulating properties, determine the failure mechanism and determine ways to prevent the failure.

        b) At the conclusion of animal experiments, analyze the implanted conductors and insulators to determine any changes in their composition and structure.

g. Based on the results obtained with the silicone and fluorocarbon polymers that have been studied, develop new materials for this application. Synthesize these candidate insulating materials and evaluate them *in-vitro*.

h. Cooperate with other investigators in the Neural Prosthesis Program by supplying samples of insulating biomaterials for biocompatibility testing and by *in-vitro* testing of up to thirty samples of up to three new insulating materials supplied from other contractors during the period of this contract as directed by the Project Officer.

i. 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.