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Example - Early Feasibility Investigational Device Exemption

IDE Section:

Manufacturing Information

14. Manufacturing Information

This section contains:

14.1. Facilities

14.1.1. Case Western Reserve University

The NNP System was conceived of, and developed at, the NNP Facilities that are based at Case Western Reserve University (CWRU). CWRU is a leading academic research institution located in Cleveland, Ohio. The primary manufacturing activity at CWRU is related to incoming inspection, storage and transfer to MHMC for surgical implantation.

The NNP Facilities includes laboratory space of over 5,500 square feet and is the site for inspection and storage of the NNP System. The NNP Quality Management System at CWRU is designed for applicability to human feasibility studies performed under IDEs. The NNP Facilities at CWRU are not ISO certified.

The NNP Team at CWRU is part of the Cleveland FES Center (FESC), which has a long history of conducting human feasibility studies related to motor neuroprostheses. The FESC is a consortium that was established in 1991 as a Center of Excellence through funding from the Dept. of Veterans Affairs Rehabilitation Research and Development Service. The FESC partner institutions include the Louis Stokes Cleveland VAMC (LSCVAMC), Case Western Reserve University (CWRU), and MetroHealth Medical Center (MHMC), a public hospital system. All clinical aspects of the study, including all surgeries and follow-up, will be performed at MHMC, a teaching affiliate of the CWRU School of Medicine.

The mission of the FESC is to perform basic and applied research for restoring individuals with central nervous system injury or disease, and to disseminate the resulting knowledge and techniques. The primary goals of the Center are to restore upper and lower extremity movement, restore trunk control and stability, restore bladder and bowel control, and provide maintenance of tissue health. To date, our clinical research has primarily concentrated on disabilities related to spinal cord injury and stroke. The FES Center is an internationally recognized leader in the development and clinical deployment of FES technologies for spinal cord injury. The following are highlights of some of the most significant accomplishments of the FESC:

- Implemented the first ever hand grasp neuroprosthesis with external control (in 1986).
- Initiated the first multi-center clinical trial of an implanted hand grasp neuroprosthesis in 1991 (under IDE G890084).
- Transferred the first generation hand grasp to industry (NeuroControl Corp.), which received PMA in 1997 (P950035).
- Implemented first ever hand grasp neuroprosthesis with an implanted controller. System can use either implanted joint angle sensor, implanted in four subjects, or myoelectric control, implanted in 13 subjects to date (under IDE G950116).
- Implemented first bilateral neuroprosthesis, giving tetraplegic subjects use of both hands, implemented in four subjects (under IDE G950116).
- Implemented first ever implanted neuroprosthesis to restore both hand and arm function in an individual with high tetraplegia. This 24-channel stimulation system includes multiple nerve cuff electrodes and is controlled via myoelectric recordings from neck and face muscles (under IDE G950116).
- Organized multicenter clinical trial of an implanted neuroprosthetic system for exercise, standing and transfers after motor complete SCI (under IDE G900108).

- Demonstrated EMG controlled stepping with an implanted neuroprosthesis for individuals with motor and sensory incomplete spinal cord injuries.
- Implanted first-ever second-generation neuroprosthesis for standing utilizing multi-contact nerve cuff electrodes and an implanted 16-channel stimulator-telemeter (under IDE G040214).
- Transferred to industry a clinical trial of neuromodulation for urge incontinence, which eventually received HDE approval (H980005 and H980008).
- Discovered frequency-dependent excitatory reflexes from pudendal nerve to bladder in animals and humans.
- Demonstrated feasibility of implanted gluteal electrical stimulation for long-term maintenance of improved regional tissue health and decreased risk of pressure ulcer development.

14.1.2. [redacted]

The implanted NNP System modules, PM1, PG4 and BP2, are manufactured at [redacted]

NOTE: At the time this IDE was written the redacted information was true; at the time of publishing this IDE via COSMIIC (2024) this manufacturer is no longer used. Implanted modules are now manufactured at Synapse Biomedical, Inc.

14.1.3. Ardiem Medical, Inc.

The implanted NNP System leads and electrodes are manufactured at Ardiem Medical, Inc. Ardiem Medical, Inc. is a full-service medical device design and manufacturing company providing complete turnkey process solutions and full-scale production capabilities. Ardiem Medical, Inc. was established in 2001 as a contract developer and manufacturer of medical devices. They are housed in an 18,000 square foot building in Indiana, Pennsylvania, and includes a Class 10,000 clean room for the manufacture of

implantable products and clean space for production and packaging. Ardiem Medical's employees have many years of experience in research, development and manufacture of medical devices, such as pacemakers, heart valves, injection ports, catheters, functional electrical stimulators, custom medical electrode leads and other prototype devices made to our customers' orders.

Ardiem Medical provides ISO compliance and process development capabilities. They possess expertise in electro-mechanical medical device manufacturing and implantable medical device manufacturing. Ardiem Medical, Inc. supplies custom electrodes, implantable devices, and surgical instruments to academic and corporate researchers in prototype and short-run production quantities. Research products are fabricated under strict quality and traceability standards for medical devices. Ardiem Medical manufactures a variety of medical devices and instruments for various customers for commercial sale.

14.1.4. Quallion, Inc.

A key component of the implanted NNP System is the Li-ion rechargeable battery housed in the power module. These batteries are manufactured at Quallion, LLC. Quallion LLC produces a number of primary and rechargeable cell and battery configurations for use in the medical, military and aerospace markets, with revenues divided evenly across these three market segments. Relevant chemistry experience includes Li ion (various species of LiCoO, LiMnCo, LiNiCoO), Li Polymer, Li Metal, CFx, SVO, LVO, and Li Air. Production capabilities range from high volume medical and military batteries to unique custom-designed aerospace batteries. Cell designs range from the world's smallest conventional lithium ion cell (a cylindrical 1.8 mAh cell) for implants to 15 and 72 Ah prismatic cells. Historical annual production rates exceed 60,000 units per year (cells and batteries combined) with the capacity to produce over 200,000 cells, making Quallion one of the largest Li ion cell manufacturers outside of Asia. The company currently employs over 85 people, with a large engineering department capable of supporting multiple research and development and prototyping projects simultaneously.

Quallion's quality development and manufacturing system is designed to meet the high reliability criteria of medical device and aerospace companies with 100% components and process traceability. All products undergo rigorous in-process checks and inspections using state-of-the-art technology and proprietary processes in micro-leak detection and electrical testing prior to receiving the final approval. Certifications include ISO 9001:2000, AS9100B (validation of Quality Management System to Aerospace standards), and ISO 13485:2003 (validation of Quality Management System to Medical Device standards).

14.1.5. [redacted]

[redacted]

NOTE: At the time this IDE was written the redacted information was true; at the time of publishing this IDE via COSMIIC (2024) this manufacturer is no longer used.

14.2. Assembly Procedures

The overall manufacturing process is overseen by the NNP Team at CWRU, but all manufacturing and assembly procedures are performed by each contractor. Each component follows a standardized manufacturing and assembly procedure. These procedures follow industry standard procedures for similar medical devices. Detailed manufacturing assembly procedures are outlined in Figures 1 through 5 on the following pages.

Figure 1. Assembly process for the Power Module (PM1).

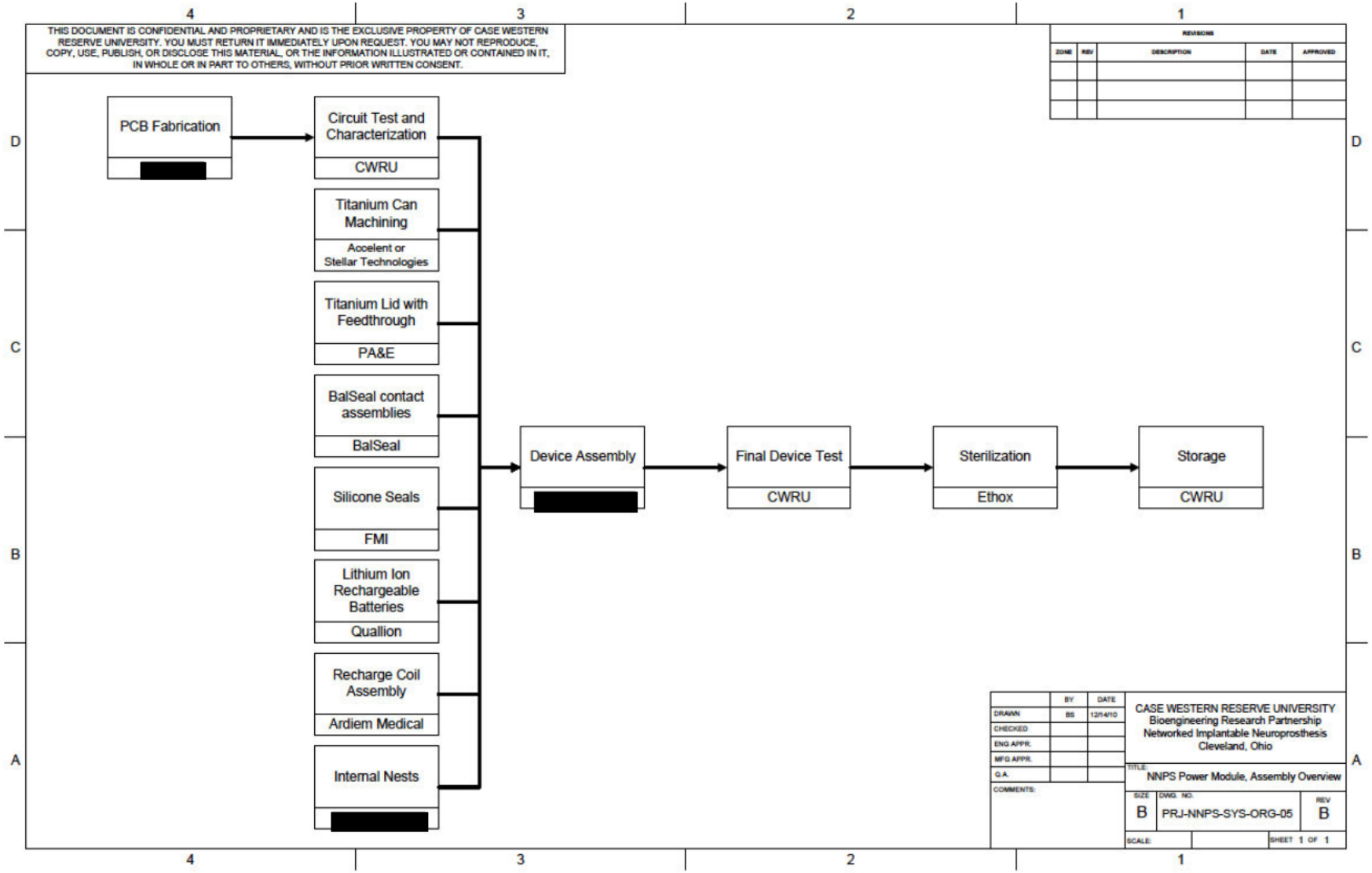


Figure 2. Assembly process for the remote modules (PG4 and BP2).

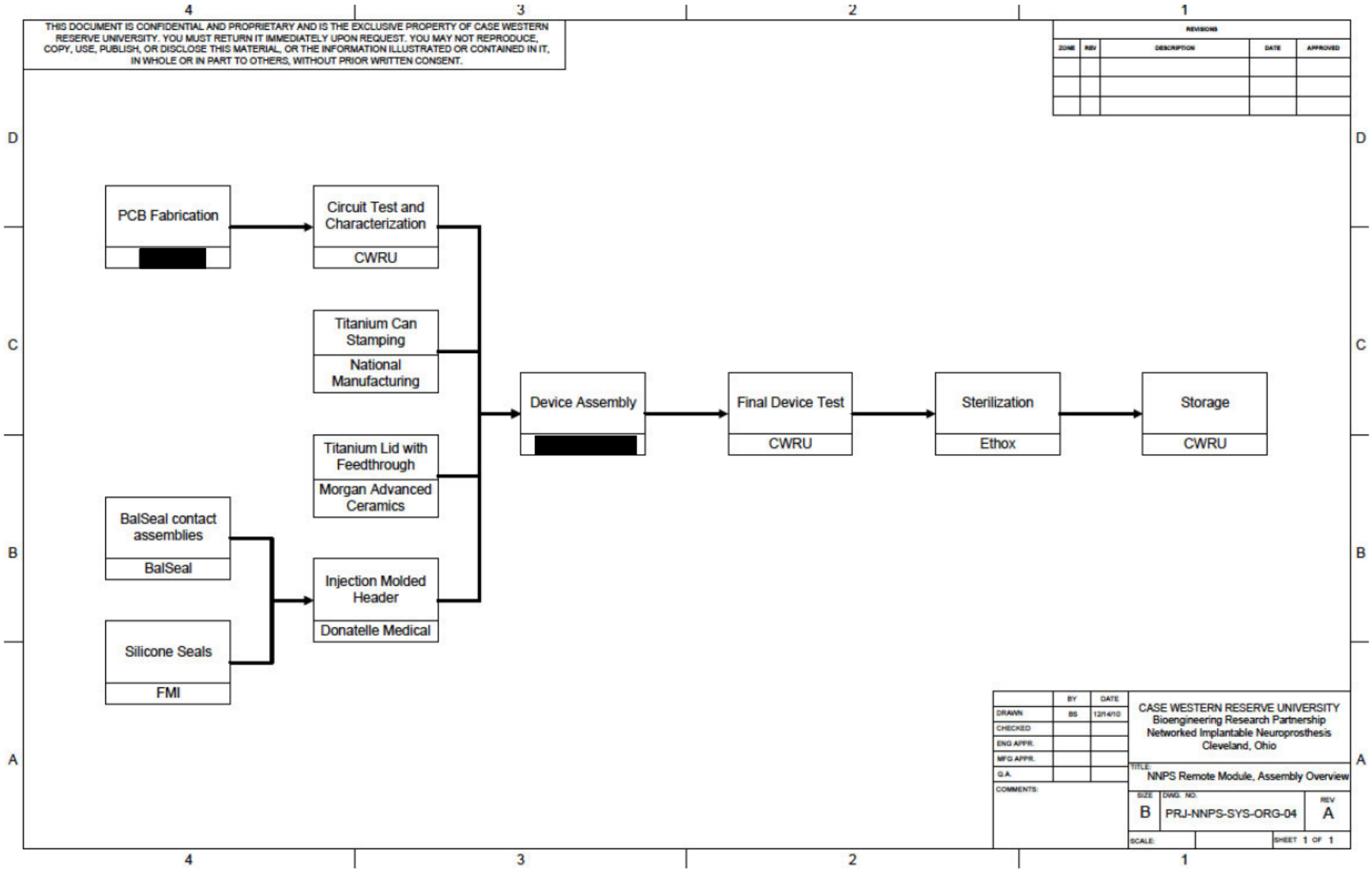


Figure 3. Assembly process for the all stimulating and recording electrodes.

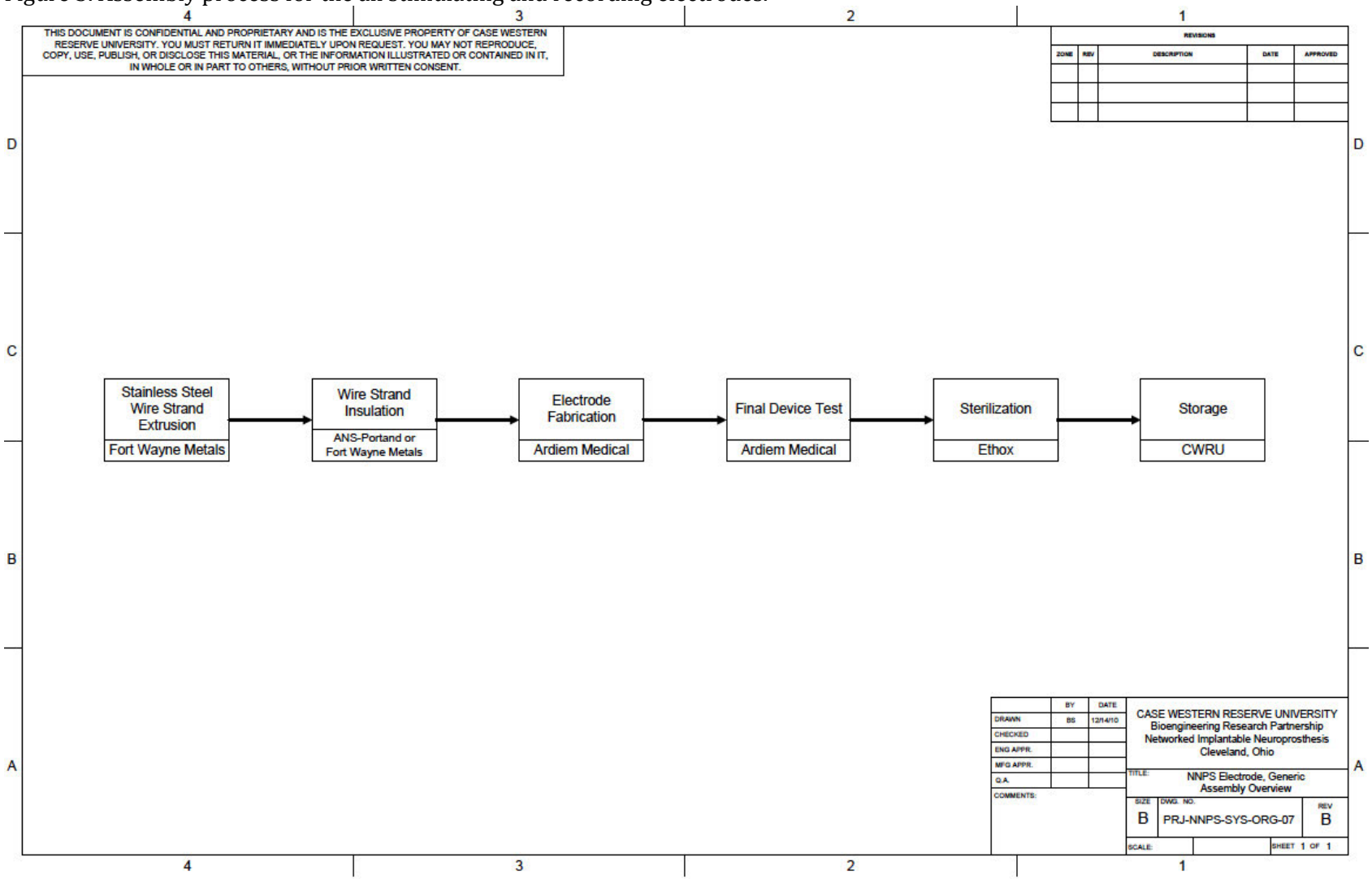


Figure 4. Assembly process for the network cable (NC2).

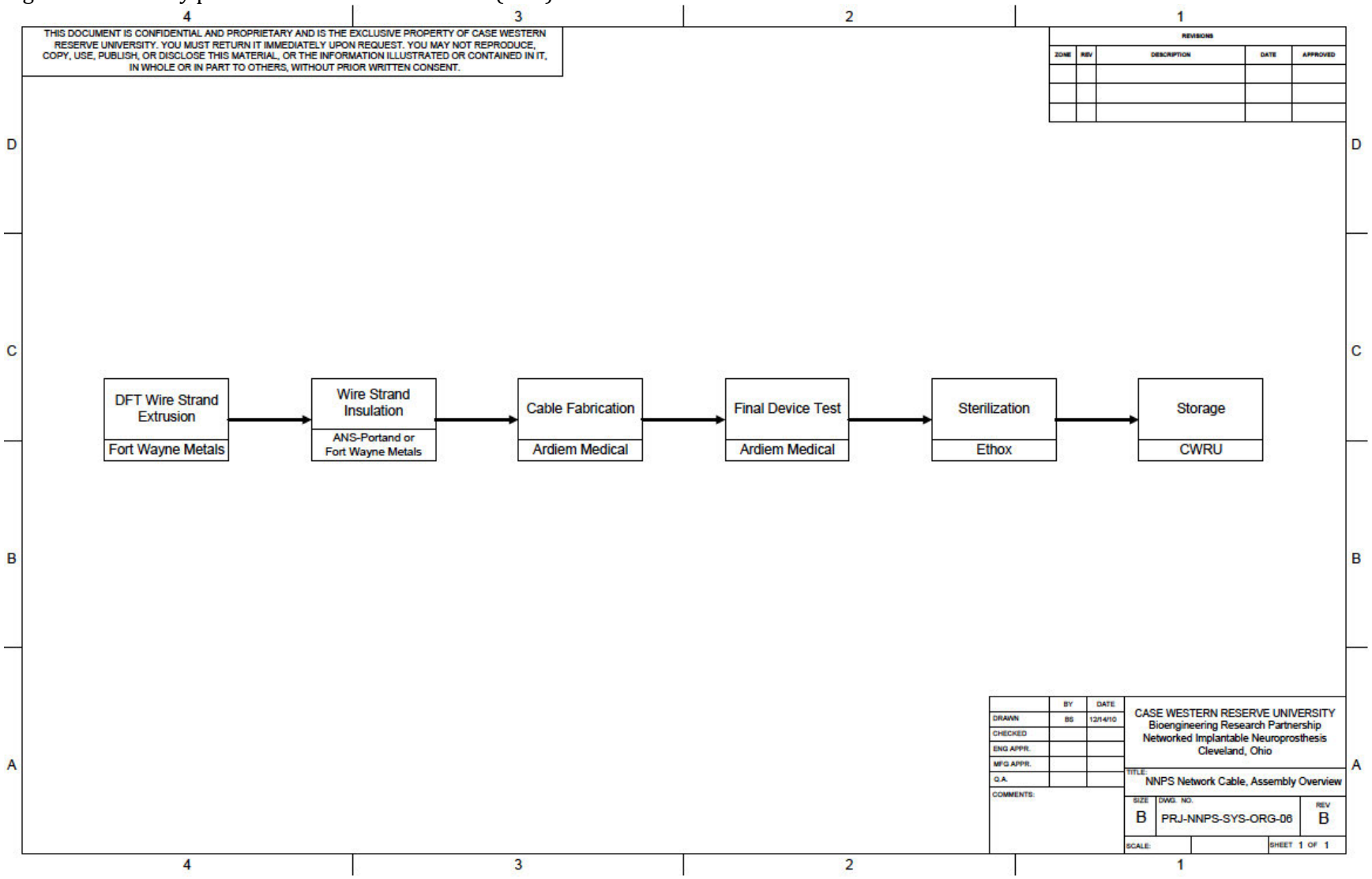
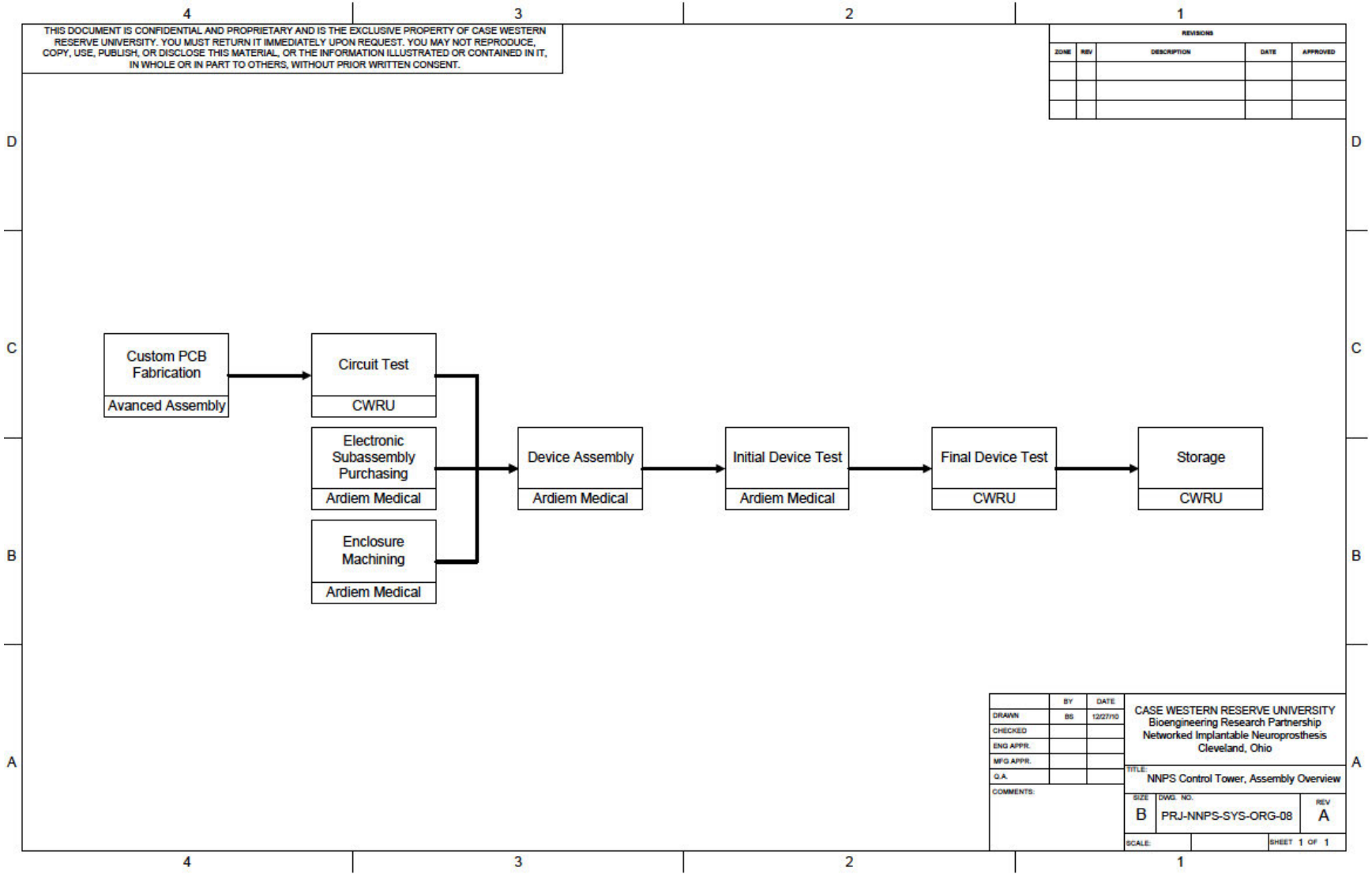


Figure 5. Assembly process for the Control Tower (CT1).



14.3. Quality System Summary

The NNP Investigative Team at CWRU focuses on early stage feasibility studies, typically with a relatively small number of subjects. As a result, the number of devices produced is small and subject to design improvements during the study. Frequently we perform 100% testing on all devices. Further, our team consists of highly skilled and experienced implant design engineers and technicians. This environment impacts the overall quality system development.

The NNP Quality System is designed around the peer-review process common to academic research groups. As an academic research group, supported almost entirely by peer-reviewed research grants (typically NIH, VA, FDA), all projects undergo external peer-review prior to initiation. Therefore, the first step in our Quality System generally begins with the funding of a proposal. Proposals typically outline design requirements and study protocols. These form the starting point for documentation related to Design Control, which is the focus of our Quality System. In general, the final output of our research culminates in the preparation of one or more manuscripts for scientific peer-review and publication in the scientific literature. These manuscripts typically form the final documentation for the outcomes of our studies.

14.3.1. Design Control

The design of the NNP System was developed, and is controlled, by the NNP Team at CWRU. Design controls used for the device are currently being (or have been) phased in to meet the requirements of the quality system regulation. During the initial stages of the project, a project plan was developed through the grant submission process to identify resources and activities necessary to implement and complete the project.

The NNP Design Control process follows the standard components as described in 21 CFR 820.30, including Design Input, Design Output, Design Review and Design Verification. The Product Development Cycle begins with Concept and Feasibility phases, which are the research activities that can result in a Design Requirements Document. Design Input will generally be prepared during the Concept and Feasibility phases. It will result in the preparation of the Design Requirements Document, which establishes the design criteria for the product and/or service. After issuance of the Design Requirements Document, all released documentation will be subject to change control. Typically, the first draft of the Design Requirements Document is the peer-reviewed and funded proposal, which is further developed as necessary through the product planning, development and prototype-production phases, resulting in the Design Output. The Design output will include prototype(s), documentation including test specifications, drawings, parts lists, etc., and engineering reports. At designated times during all phases of the Product Development Cycle, Design Reviews may be conducted and reports of their conclusions will be included and/or referenced in the Design History File. Additional reviews also occur as part of the peer-review funding process, include grant progress reports, presentation at scientific conferences, and manuscript submission. Prototype verification will be conducted and technical reports prepared during the development and prototype-production phases. Process validation will be conducted and reported also, if applicable. Design Validation is generally performed at the final peer review level as part of the manuscript review process.

14.3.2. Document Controls

Document Control is conducted to control and maintain all documentation and data generated and used in the quality systems. The NNP Team at CWRU will approve all documents and data prior to their issuance and use. In addition, their issuance and use will be controlled. The NNP Quality System documentation will include but is not limited to: The Quality System Manual, Policies, Standard Operating Procedures, Work Instructions, Design documentation including the Design History File, Device History Records, and Device Master Records. In order to facilitate electronic document control, a secure document control software is utilized (KnowledgeTree, Knowledge Tree, Inc, Raleigh, NC).

14.3.3. Additional Controls

Nearly all fabrication of the NNP System occurs at [redacted] and Ardiem Medical; with purchase of the key component, the Li-ion battery, from Quallion, Inc.. Each of these partners maintain a full Quality System and maintain ISO compliance, as described in [redacted]; Ardiem Medical, Inc.; [redacted] and Quallion, Inc.. This includes: Design Controls and DHF Management, Design Verification Planning and Testing, FMEA and Risk Analysis Documentation, Equipment and Process Qualification, Process Validation, and Lot History Record Management.

The NNP Team at CWRU performs Inspection and Testing of incoming components. It establishes and maintains documented procedures for inspection and testing activities in order to verify that the specified requirements for the product are met. The required inspection and testing, and the established records, are detailed in quality plans or other documented procedures and work instructions. All materials and products will be handled, stored, packaged, and delivered in a manner that ensures integrity, controls distribution, and maintains quality through delivery. The NNP Team at CWRU also maintains Control of Inspection, Measuring, and Test Equipment. This includes calibration, and maintenance of inspection, measuring and test equipment to demonstrate the conformance of product to the specified requirements. Equipment will be used and cared for in a manner that ensures that the measurement uncertainty is known and is consistent with the required capability. Equipment used in the NNP Facilities at CWRU will be subject to periodic calibration, where appropriate.