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Example - Early Feasibility Investigational Device Exemption

IDE Section:

Appendix D – Biocompatibility

D. Appendix D – Biocompatibility

This section contains:

D.1. Overview and Conclusions

The NNP utilizes only established materials with demonstrated biocompatibility and an existing track record of human implantable use over several decades, including common materials used in pacemakers, spinal cord stimulators and deep brain stimulators. Review of our own experience with these materials, and review of the medical literature, reveals no significant adverse biocompatibility reported with these materials as utilized in the NNP System. The specific physical configuration, manufacturing procedures, and sterilization procedures used by the various NNP System processes may be different between than those of existing clinical use; however, these differences are consistent with common differences between implantable devices where biocompatibility has been maintained.

We anticipate design changes based on the Early Feasibility Study. These changes are not likely to include changes in materials (although conceivable), but are almost certain to include changes to the specific manufacturing procedures of the implanted components. For the materials utilized in the NNP System, adverse tissue reactions are extremely unlikely and the risk is very low that the processing methods for any of the materials will result in an adverse reaction. Thus, biocompatibility studies, such as long-term implantation, are expected to be confirmatory in nature, rather than providing new data.

Previous clinical studies conducted at CWRU using our IRS-8, IST-10, and IST-12 implantable technologies use many of the same materials as the NNP System, with identical processing. The previous clinical studies were conducted under our own IDEs: G890084, G900108, G950116, and G040214. In addition, the CWRU Cleveland FES Center has obtained authorization from Invacare Corp. to reference the contents of the Freehand System Premarket Approval Application (P950035) and Supplements for the purpose of reviewing materials and associated biocompatibility testing of both skin contact and implanted system components.

For every direct-contact implantable material, we have supported our assertion of material biocompatibility in one or more of the following ways: 1) by characterizing biocompatibility through cytotoxicity testing (tests passed); 2) by establishing the material's prior use in our own previously approved IDEs; and/or 3) by providing right-of-reference letters to materials Master Files. **Therefore, based on our Risk Analysis and Device Evaluation Strategy, we conclude that for the purposes of conducting an Early Feasibility study on a limited number of subjects, no additional biocompatibility testing is necessary *at this stage*. Full biocompatibility testing will be completed after refining the manufacturing processes for the technology.**

D.2. List of Direct-Contact Implantable Materials

Only materials that are in direct contact with tissue are listed. There are several component-materials that can be discernible in the various implantable structures that are visually transparent - such as the transparent headers and transparent lead wires - these indirect-contact materials are totally encased within a direct-contact material, and cannot contact tissue except under catastrophic failure condition. Hence, these materials are not listed. Similarly, materials that are inside hermetically sealed, metallic cases are not listed.
All direct-contact materials contact muscle, nerve, or connective tissue; there is no direct blood contact by any implantable components in the NNP.

D.2.1. Power Module Direct-Contact Materials

Common Name	Manuf. Name	Scientific Name or Standard Reference	Used in	Function	Biocompatibility Reference	Data Sheet or Test Report
Titanium Grade 23	6AL-4V ELI	Titanium Base Alloy ASTM F136	Capsule	Provides protection for internal electronic components, such as PCBs, batteries, recharge coil.	Marketed as "Implantable Grade" when assayed and certified to ASTM F136.	Titanium Base Alloy Ti-6Al-4V ELI (Grade 23) NAMSA Test Report - Cytotoxicity Study of Power Module Capsule
Tecothane	Lubrizol TT-1075D-M	Aromatic polyether-based thermoplastic polyurethane (TPU)	Capsule header	Encapsulant protection for female interconnect assembles, wireless antenna, and feedthough wires.	Previous use in Guidant Corporation, Easytrak 3 LV1, P10012/S025, P050046 We do not possess a right-of-reference letter for this application.	Lubrizol Corporation - Evaluation of Biocomatibility and Biostability of Tecothane NAMSA Test Report - Cytotoxicity Study of Remote Module Assembly
Fast-cure Silicone Adhesive	NuSil MED3-4213		Header adhesion and back-fill	Adhesive used to attach header to metal capsule. Also used as sealant to fill weld access points after the header assembly is attached.	Materials Master File: MAF-1522	NuSil Technology MED3-4213 Fast-Cure Silicone Adhesive
Low Viscosity Silicone Elastomer	NuSil MED-6215		Header back-fill	Used as sealant to fill weld access points and vent holes after the header assembly is attached.	Materials Master File: MAF-950	NuSil Technology MED-6215 Low Viscosity Silicone Elastomer
Polyester Reinforced	Specialty Silicone		Suture skirt	Allows the use of non-absorbable sutures to	Previous use under our own IDEs: G890084, G900108, G950116,	Custom fabricated material

Silicone Sheeting	Fabricators Silicone SSF-METN-750 Polyester fabric SSF-FMR-1160			anchor the capsule to the underlying tissues.	and G040214	
Silicone Adhesive	NuSil MED-1137		Suture skirt	Adhesive used to adhere suture skirt to capsule.	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-1137 Fast-cure Medical Adhesive
Silicone Primer	NuSil MED6-161		Suture skirt	Used to promote adhesion of suture skirt to capsule.	Materials Master File: MAF-1398	NuSil Technology MED6-161 Silicone Primer

D.2.2. Remote Module (all types) Direct-Contact Materials

Common Name	Manufacturer Name	Scientific Name or Standard Reference	Used in	Function	Biocompatibility Reference	Data Sheet or Relevant Literature
Titanium Grade 1		Commercially Pure Titanium ASTM F67	Capsule	Provides protection for internal electronic components.	Marketed as "Implantable Grade" when assayed and certified to ASTM F67	Titanium, Commercially Pure Grade 1
Titanium Grade 2		Commercially Pure Titanium ASTM F67	Capsule feedthrough assembly	Provides protection for internal electronic components.	Marketed as "Implantable Grade" when assayed and certified to ASTM F67 Previous use under IDEs: G890084, G900108, G950116, and G040214 Previous use in NeuroControl, Freehand, PMA P950035	Titanium, Commercially Pure Grade 2
Tecothane	Lubrizol TT-1075D-M	Aromatic polyether-based thermoplastic polyurethanes (TPU)	Header	Encapsulant protection for female interconnect assembles, wireless antenna, and feedthough wires.	CWRU tested for cytotoxicity	NAMSA Test Report - Cytotoxicity Study of Remote Module Assembly
UV-cure Acrylate Adhesive	EMIUV mCast 710-2K		Header adhesion and back-fill	Adhesive used to attach header to metal capsule. Sealant used to fill weld access points after assembly.	Certified to USP Class VI CWRU tested for cytotoxicity	EMIUV mCast 7105-2K Adhesive Product Sheets, USP Test Reports, & Cytotoxicity Test Reports NAMSA Test Report - Cytotoxicity Study of Remote Module Assembly
Polyester	Specialty		Suture skirt	Allows the use of non-	Previous use under our own IDEs:	Custom fabricated

reinforced silicone sheeting	Silicone Fabricators Silicone SSF-METN-750 Polyester fabric SSF-FMR-1160			absorbable sutures to anchor the capsule to the underlying tissues.	G890084, G900108, G950116, and G040214	material
Silicone Adhesive	NuSil MED-1137		Suture skirt	Adhesive used to adhere suture skirt to capsule.	Unrestricted material, manufacturer Master File at FDA Previous use under IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-1137 Fast-cure Medical Adhesive
Silicone Primer	NuSil MED6-161		Suture skirt	Used to promote adhesion of suture skirt to capsule.	Materials Master File: MAF-1398	NuSil Technology MED6-161 Silicone Primer

D.2.3. Electrode-Cable and Network-Cable Direct-Contact Materials

Common Name	Manufacturer Name	Scientific Name or Stand Ref.	Used in	Function	Biocompatibility Reference	Data Sheet or Relevant Literature
Silicone Elastomer	NuSil MED-4750		Insulating tubing	Provides protection for the insulated, stranded conductors.	Materials Master File: MAF-500	NuSil Technology MED-4750 Silicone Elastomer
Liquid Silicone Rubber	NuSil MED-4850		Strain relief with dual o-ring	Provides stain-relieving transition from interconnect pin to cable body, and sealing of interconnect pin assembly into receptacle.	Materials Master File: MAF-692	NuSil Technology MED-4840 Liquid Silicone Rubber NuSil Technology MED-4850 Liquid Silicone Rubber
Pigment	NuSil Med-4800 color pigments for Liquid Silicone Elastomers		Strain relief with dual o-ring	Provides color-coding to identify interconnect function.	Materials Master Files: MAF-1434, MAF-1435, MAF-1436, MAF-1439, MAF-1440 MAF-1441	NuSil Technology MED-4800 Color Masterbatches
Silicone Adhesive	NuSil MED-1137		General assembly	Adhesive	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-1137 Fast-cure Medical Adhesive
Low Consistency Silicone Elastomer	NuSil MED-4211		General assembly	Adhesive	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-4211 Low Consistency Silicone Elastomer

D.2.4. Intramuscular Stimulating-Electrode and Recording-Electrode Direct-Contact Materials

Common Name	Manufacturer Name	Scientific Name or Standard Reference	Used in	Function	Biocompatibility Reference	Data Sheet or Relevant Literature
Stainless Steel 316LVM		Stainless Steel ASTM F138	Tissue interfaces	Stimulating and recording surfaces	Marketed as "Implantable Grade" when assayed and certified to ASTM F138 Previous use under our own IDEs: G890084, G900108, G950116, and G040214	Stainless Steel, 316LVM
Monofilament Polypropylene	Ethicon Prolene Non-absorbable Suture		Tissue anchors	Barb used to mechanically anchor the electrode within the muscle tissues	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	
Silicone Adhesive	NuSil MED-1137		Over-molding	Anchors exposed electrode contacts to silicone tubing	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-1137 Fast-cure Medical Adhesive

D.2.5. Epimysial Stimulating-Electrode and Recording-Electrode Direct-Contact Materials

Common Name	Manufacturer Name	Scientific Name or Standard Reference	Used in	Function	Biocompatibility Reference	Data Sheet or Relevant Literature
Platinum 10% Iridium	Pt10Ir	Platinum Base Alloy	Tissue interfaces	Stimulating surfaces	Previous use under our own IDEs: G890084, G900108, G950116, and G040214 Previous use in NeuroControl, Freehand, PMA P950035	
Polyester reinforced silicone sheeting	Specialty Silicone Fabricators Silicone SSF-METN-750 Polyester fabric SSF-FMR-1160		Electrode backing and suture skirt	Allows the use of non-absorbable sutures to anchor the capsule to the underlying tissues.	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	Custom fabricated material
Low Consistency Silicone Elastomer	NuSil MED-4211		Over-molding	Encapsulates the electrode termination and backing materials	Previous use under our own IDEs: G890084, G900108, G950116, and G040214	NuSil Technology MED-4211 Low Consistency Silicone Elastomer

D.2.6. Port-Plug Direct-Contact Materials

Common Name	Manufacturer Name	Scientific Name or Standard Reference	Used in	Function	Biocompatibility Reference	Data Sheet or Relevant Literature
Silicone Elastomer	NuSil MED-4750		Insulating tubing	Provides protection for the insulated, stranded conductors.	Materials Master File: MAF-500	NuSil Technology MED-4750 Silicone Elastomer
Liquid Silicone Rubber	NuSil MED-4850		Strain relief with dual o-ring	Provides stain-relieving transition from interconnect pin to cable body, and sealing of interconnect pin assembly into receptacle.	Materials Master File: MAF-692	NuSil Technology MED-4850 Liquid Silicone Rubber
Pigment	NuSil Med-4800 family of color pigments for Liquid Silicone Elastomers		Dual o-ring and plug body	Provides color-coding to identify interconnect port function.	Materials Master Files: MAF-1434 MAF-1435 MAF-1436 MAF-1439 MAF-1440 MAF-1441	NuSil Technology MED-4800 Color Masterbatches

D.3. NAMSA Cytotoxicity Study – Power Module Capsule

Confidential NAMSA Biocompatibility test reports for the Power Module and Remote Module Assembly (pgs. D12-D25) have been removed. New biocompatibility testing is being conducted at the time of this IDE release by COSMIIC and will be released open-source once completed.

D.5. Right of Reference to Materials Master Files

In the pages that follow are right-of-reference letters for:

- NuSil MED-4750 Materials Master File MAF-500
- NuSil MED-4800-1 Materials Master File MAF-1434
- NuSil MED-4800-2 Materials Master File MAF-1435
- NuSil MED-4800-3 Materials Master File MAF-1436
- NuSil MED-4800-6 Materials Master File MAF-1439
- NuSil MED-4800-7 Materials Master File MAF-1440
- NuSil MED-4850 Materials Master File MAF-692
- NuSil MED-6215 Materials Master File MAF-950
- NuSil MED1-4800-7 Materials Master File MAF-1441
- NuSil MED3-4213 Materials Master File MAF-1522
- NuSil MED6-161 Materials Master File MAF-1398
- NuSil MED-4211 Materials Master File MAF-612
- NuSil MED-1137 Materials Master File MAF-586
- NuSil MED-4840 Materials Master File MAF-682

Right of Reference letters have been excluded for privacy reasons.