Task 1.16: FDA IDE submission for (b)(4)

(b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.3: Restore sexual function (b)(4)
  - Restoring penile erection in 2 cats by (b)(4) stimulation (b)(4)
- Task 1.4: Implantable pulse generator with (b)(4)
  - Integrate pulse generator circuit into can (b)(4)
  - Final PC test application with wireless board connectivity (b)(4)
  - Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  - First prototypes (b)(4) delivered for test (b)(4)
- Task 1.8: Physician/Investigator controller for (b)(4)
  - Evaluation board fabricated/assembled and initial evaluation complete (b)(4)
  - Integration with a simple enclosure with display and firmware (b)(4)
- Task 1.9: Patient controller for (b)(4)
  - Verification testing completed (b)(4)

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Work Plan for Next 4 Weeks (b)(4)

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  Continue to prepare IDE application for (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1645

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [11/1/2021] – [11/30/2021]

11/30/2021

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1649

Overview – Technical Update

- Penile erection study was performed in a total of 8 cats. Data were analyzed and summarized. A manuscript for penile erection study is ready for submission (attached).
- The manuscript for defecation study was accepted for publication on American Journal Physiology - Gastrointestinal and Liver Physiology.
- The GUI controller successfully communicates (b)(4) wirelessly (b)(4) more (b)(4) PCBAs have been ordered.
- (b)(4)
- The (b)(4) schematic has been reduced as much as possible to fit inside the (b)(4)
- The (b)(4) can supplier will deliver (b)(4) samples (b)(4)
- (b)(4)
- The (b)(4) design was reviewed by the internal team and sent out for (b)(4) quotation. The feedback from the (b)(4) was incorporated into the design changes.
- The complete (b)(4) manufacturing process continues to be improved, inspected and tested. The (b)(4) (b)(4) has been better defined.
- (b)(4) is currently being coated with (b)(4)
- Thermaquil is drafting IDE in response to FDA feedback on IDE Pre-Sub #2
- Protocol (b)(4) updated in response to FDA feedback (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1650

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.3: Restore sexual function [redacted]
  - Restoring penile erection in 2 cats by [redacted]
- Task 1.4: Implantable pulse generator [redacted]
  - Integrate pulse generator circuit into can [redacted]
  - Final PC test application with wireless board connectivity [redacted]
  - Full integration and test completed for initial prototype [redacted]
- Task 1.7: [redacted] electrodes for human use [redacted]
  - First prototypes of [redacted] delivered for test [redacted]
- Task 1.8: Physician/Investigator controller for [redacted]
  - Evaluation board fabricated/assembled and initial evaluation complete [redacted]
  - [redacted]
  - Integration with a simple enclosure with display and firmware [redacted]
- Task 1.9: Patient controller for [redacted]
  - Verification testing completed [redacted]

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1653

4 Week Work Plan from Previous Report

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol for (b)(4)
  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  Continue to prepare IDE application for (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1654

COVID related updates

- Current MSR period – (b)(4) (11/1/2021-11/30/2021)
  - (b)(4)

Big Wins

GI-00269-2021R1 Accept for publication

(b)(6)@msubmit.net (b)(6)@msubmit.net>

Mon 11/8/2021 9:33 PM

To: (b)(6)@pitt.edu>

Cc: (b)(6)@uic.edu (b)(6)@uic.edu>

Dear (b)(6)

I am pleased to inform you that your letter GI-00269-2021R1, entitled "Defecation Induced by Stimulation of Sacral S2 Spinal Root in Cats" has been accepted for publication in the next available issue of the American Journal of Physiology - Gastrointestinal and Liver Physiology. Accepted Letters and any accompanying Reply, if written, are published together only after both are finalized in the next available issue.

Thank you for submitting your work to The American Journal of Physiology.

Sincerely,

(b)(6)

American Journal of Physiology-Gastrointestinal and Liver Physiology

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1656

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 10/31/2021

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.3 Restore sexual function (b)(4) (b)(4)		(b)(4)				Milestone 1.2.3(1-4) – Deliverable 1.2.3	
1.3 Test Bed Environment (b)(4)							
1.3.4 Integration of EPG in enclosure with firmware and (b)(4) connectivity (b)(4)		(b)(4)				Milestone 1.3.4	
1.4 Implantable pulse generator with (b)(4)							
1.4.3 Integrate pulse generator circuit into can (b)(4)		(b)(4)				Milestone 1.4.3 – Deliverable 1.4	
1.4.4 Final PC test application with wireless board connectivity (b)(4)						Milestone 1.4.4 – Deliverable 1.4	
1.4.5 Full integration and test completed for initial prototype (b)(4)						Milestone 1.4.5 – Deliverable 1.4	
1.6 External pulse generator for (b)(4)							
1.6.3 System verification completed (b)(4)		(b)(4)				Milestone 1.6.3 – Deliverable 1.6.1 – Deliverable 1.6.2	
1.6.4 Documentation Supporting the IDE submission (b)(4)						Milestone 1.6.4 – Deliverable 1.6.1	
1.6.5 Build sets of (b)(4) to conduct GLP safety study in pigs in (b)(4)						Milestone 1.6.5 – Deliverable 1.6.2	
1.7 (b)(4) electrodes for human use (b)(4)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)		(b)(4)				Milestone 1.7.3 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1657

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 10/31/2021

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.8 Physician/Investigator controller for (b)(4)							(b)(4)
1.8.2 Evaluation board fabricated/assembled and initial evaluation complete (b)(4)	(b)(4)					Milestone 1.8.1	
1.8.3 Integration with a simple enclosure with display and firmware (b)(4)						Milestone 1.8.1	
1.9 Patient controller for (b)(4)							
1.9.2 Verification testing completed (b)(4)	(b)(4)					Milestone 1.9.2 – Deliverable 1.9	
1.16 FDA IDE Submission (b)(4)							
1.16.1 FDA IDE application for the (b)(4) is submitted	(b)(4)					Milestone 1.16 – Deliverable 1.16	
1.13 Early feasibility human clinical protocol for (b)(4)							
1.13 Early feasibility human clinical protocol (b)(4)	(b)(4)					Milestone 1.13 – Deliverable 1.13	
1.11 GLP animal study (b)(4)							
1.11 GLP animal study						Milestone 1.11 – Deliverable 1.11	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1658

Technical Progress Summary

- Animal studies to restore penile erection are performed in 8 cats. (b)(4) (b)(4) is most effective in inducing (b)(4) but (b)(4)
- A manuscript for penile erection studies is ready for submission (attached).
- The GUI successfully controlled the (b)(4) wirelessly (b)(4)
- The (b)(4) schematic has been reduced as much as possible to fit inside the (b)(4)
- The (b)(4) can supplier expects to deliver samples by (b)(4)
- (b)(4)
- The (b)(4) design was reviewed by the internal team and sent out for (b)(4) The feedback from the (b)(4) was incorporated into the design changes.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. The (b)(4) has been better defined.
- (b)(4) is currently being coated with (b)(4)
- Thermaquil is incorporating specific FDA feedback in IDE, clinical trial protocol, informed consent, and (b)(4)

Task 1.2.3 Restore Sexual Function

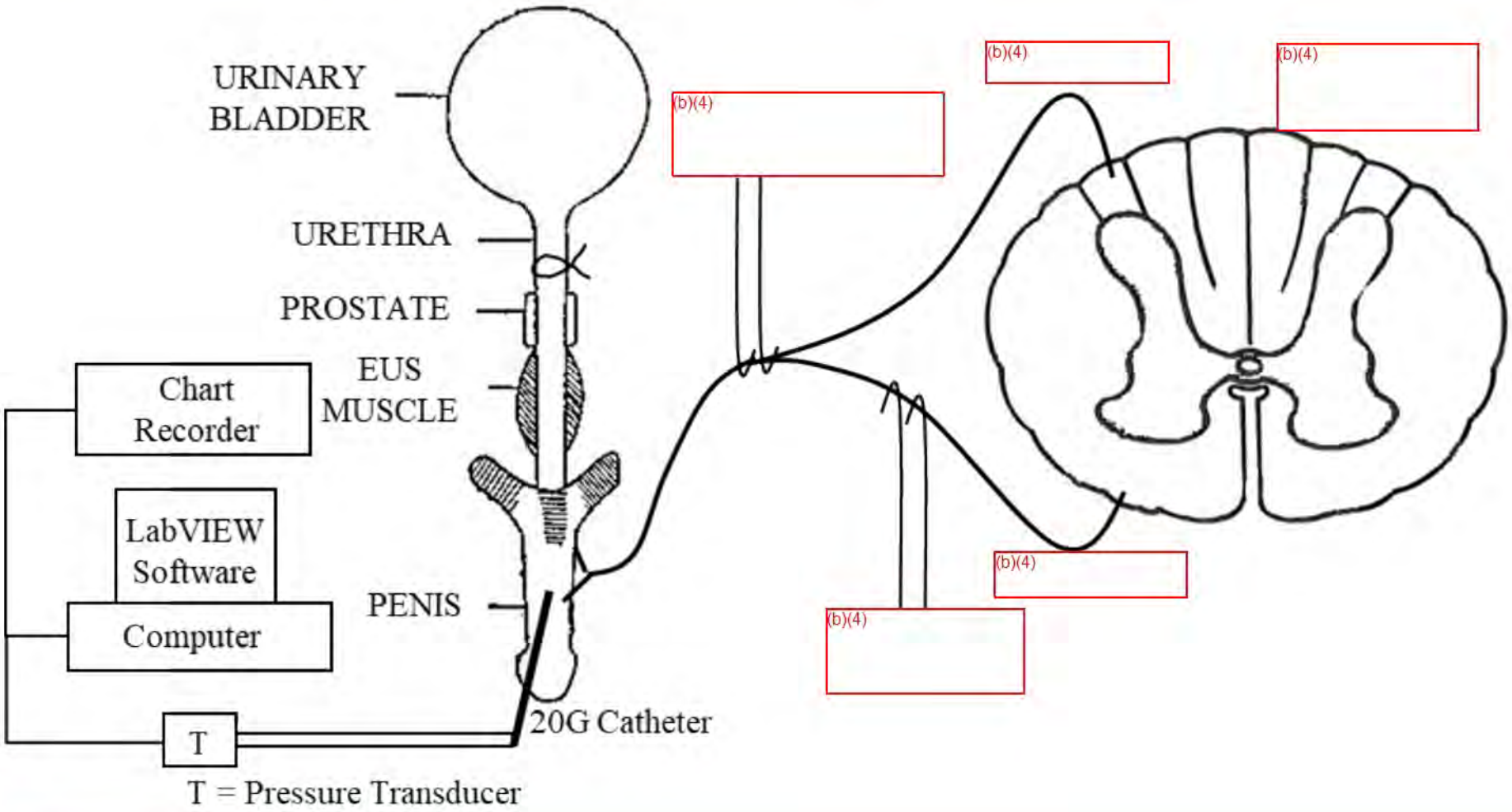


Figure 1. (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1660

Task 1.2.3 (b)(4)

(b)(4)

Task 1.2.3 (b)(4)

(b)(4)

Task 1.2.3 Sustained Penile Response after SCI

(b)(4)

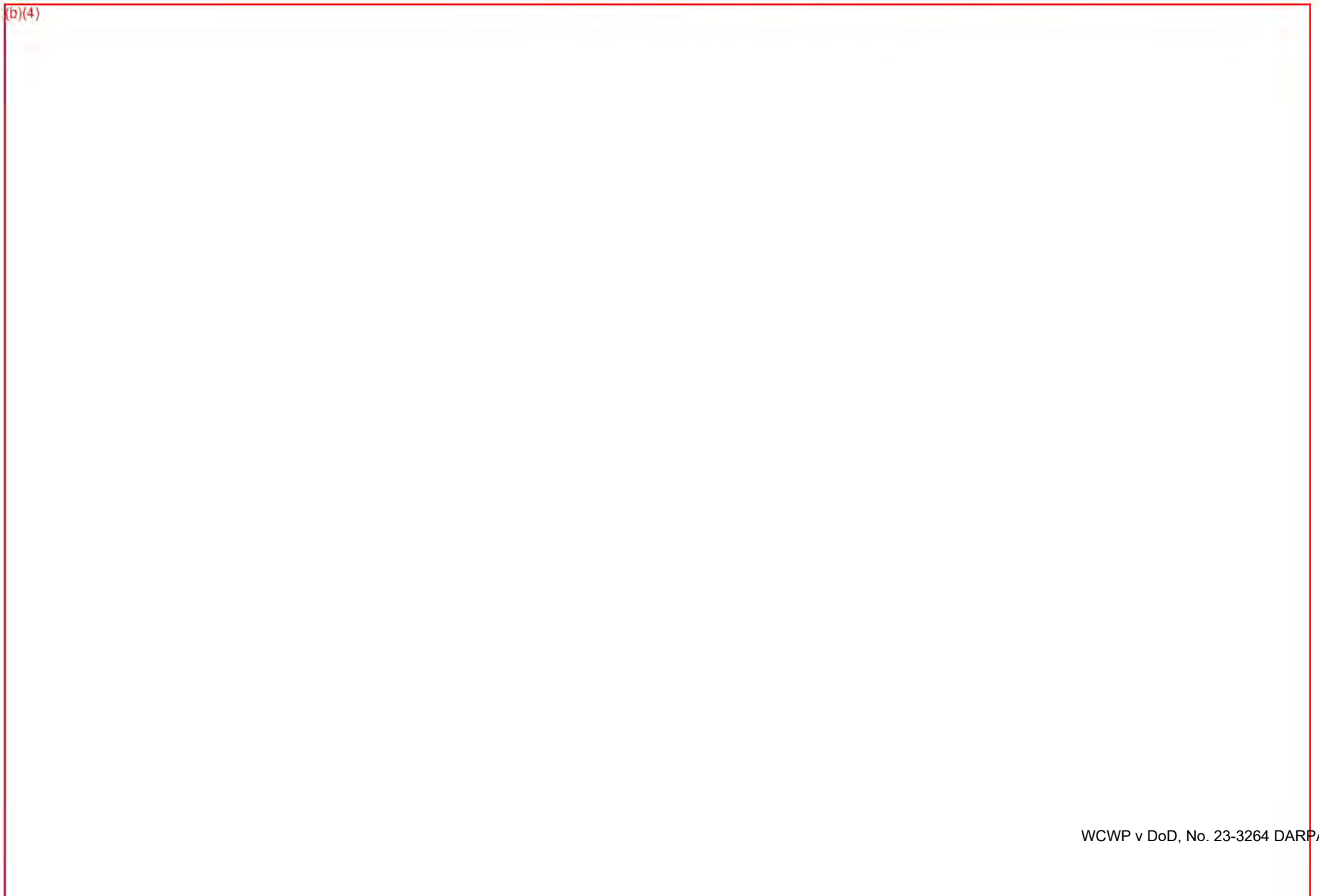
WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1663

(b)(4)

Physician GUI for IDE Study

Figure 5

(b)(4)



(b)(4)

Figure 6

(b)(4

Task 1.16: FDA IDE submission (b)(4)

(b)(4)

Figure 7: Table of contents of IDE monitoring plan draft

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.3: Restore sexual function (b)(4)
  - Restoring female sexual function in 2 cats by pudendal nerve stimulation
- Task 1.4: Implantable pulse generator (b)(4)
  - Integrate pulse generator circuit into can (b)(4)
  - Full integration and test completed for initial prototype (b)(4)
- Task 1.6: Implantable pulse generator (b)(4)
  - System verification completed (b)(4)
  - Documentation Supporting the IDE submission (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  - First prototypes (b)(4) delivered for test (b)(4)
  - Finalize design and (b)(4) production (b)(4)
  - Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.8: Physician/Investigator controller (b)(4)
  - Evaluation board fabricated/assembled and initial evaluation complete (b)(4)
  - Integration with a simple enclosure with display and firmware (b)(4)
  - Final documentation to support the FDA IDE (b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 1.9: Patient controller (b)(4)
  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  Continue to prepare IDE application for (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1668

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4), (b)(6)

Reporting Period: [12/1/2021] – [12/31/2021]

12/31/2021

Overview – Technical Update

- Sexual function study was performed in a female cat to induce vaginal contraction and secretion.
- The populated (b)(4) PCBs were received and tested. (b)(4) with enclosure assemblies were built with the newly populated PCBs.
- The (b)(4) can supplier delivered IPG can samples, (b)(4)
- (b)(4)
- Protocols for the electrical and mechanical testing (b)(4) have been written.
- All files for models, part drawings, assemblies and kits were successfully completed and released.
- The (b)(4) has been quoted, defined and logistics are being finalized. The PO will be sent out.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
- (b)(4) is currently being coated with (b)(4) and is expected to be delivered (b)(4)
- The FDA IDE submission (b)(4) is in preparation.

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1673

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.3: Restore sexual function (b)(4)
  - Restoring female sexual function in 2 cats by pudendal nerve stimulation - (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  - Integrate pulse generator circuit into can (b)(4)
  - Full integration and test completed for initial prototype (b)(4)
- Task 1.6: External pulse generator (b)(4)
  - System verification completed (b)(4)
  - Documentation Supporting the IDE submission (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  - First prototypes of (b)(4) delivered for test (b)(4)
  - Finalize design and (b)(4) production (b)(4)
  - Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)

Task 1.8: Physician/Investigator controller (b)(4)

- Evaluation board fabricated/assembled and initial evaluation complete (b)(4)

(b)(4)

- Integration with a simple enclosure with display and firmware (b)(4)
- Final documentation to support the FDA IDE as an accessory device (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1676

4 Week Work Plan from Previous Report

- Task 1.9: Patient controller (b)(4)
  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 1.11: GLP animal study (b)(4))
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol for (b)(4)
  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  Continue to prepare IDE application (b)(4)

COVID related updates

- Current MSR period – (b)(4) (12/1/2021-12/31/2021)
  - (b)(4)

Big Wins

Nothing to report

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 12/31/2021

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.3 Restore sexual function (b)(4) (b)(4)	(b)(4)					Milestone 1.2.3(1-4) – Deliverable 1.2.3	
1.4 Implantable pulse generator with (b)(4)							
1.4.3 Integrate pulse generator circuit into can (b)(4)	(b)(4)					Milestone 1.4.3 – Deliverable 1.4	
1.4.5 Full integration and test completed for initial prototype (b)(4)						Milestone 1.4.5 – Deliverable 1.4	
1.6 External pulse generator for (b)(4)							
1.6.3 System verification completed (b)(4)	(b)(4)					Milestone 1.6.3 – Deliverable 1.6.1 – Deliverable 1.6.2	
1.6.4 Documentation Supporting the IDE submission (b)(4)						Milestone 1.6.4 – Deliverable 1.6.1	
1.7 (b)(4) **electrodes for human use** (b)(4)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1680

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 12/31/2021

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.8 Physician/Investigator controller	(b)(4)			(b)(4)			(b)(4)
1.8.2 Evaluation board fabricated/assembled and initial evaluation complete	(b)(4)					Milestone 1.8.1	
1.8.3 Integration with a simple enclosure with display and firmware						Milestone 1.8.1	
1.8.4 Final documentation to support the FDA IDE as an accessory device						Milestone 1.8.4 – Deliverable 1.8	
1.9 Patient controller	(b)(4)						
1.9.2 Verification testing completed	(b)(4)					Milestone 1.9.2 – Deliverable 1.9	
1.10 Software Development Kit (SDK)	(b)(4)						
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
1.16 FDA IDE Submission	(b)(4)						
1.16.1 FDA IDE application for the (b)(4) is submitted	(b)(4)					Milestone 1.16 – Deliverable 1.16	
1.13 Early feasibility human clinical protocol	(b)(4)						
1.13 Early feasibility human clinical protocol	(b)(4)					Milestone 1.13 – Deliverable 1.13	
1.11 GLP animal study	(b)(4)						
1.11 GLP animal study						Milestone 1.11 – Deliverable 1.11	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1681

Technical Progress Summary

- (b)(4) nerve stimulation successfully induced (b)(4) and improved (b)(4) by (b)(4)
- (b)(4) with enclosure assemblies were built with the newly populated PCBs for testing.
- The (b)(4) can supplier delivered IPG can samples, (b)(4)
- (b)(4)
- All files for models, part drawings, assemblies and kits were successfully completed and released.
- The (b)(4) design has been quoted, defined and logistics are being finalized.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
- The FDA IDE submission (b)(4) is in preparation.

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1682

Task 1.2.3 (b)(4)

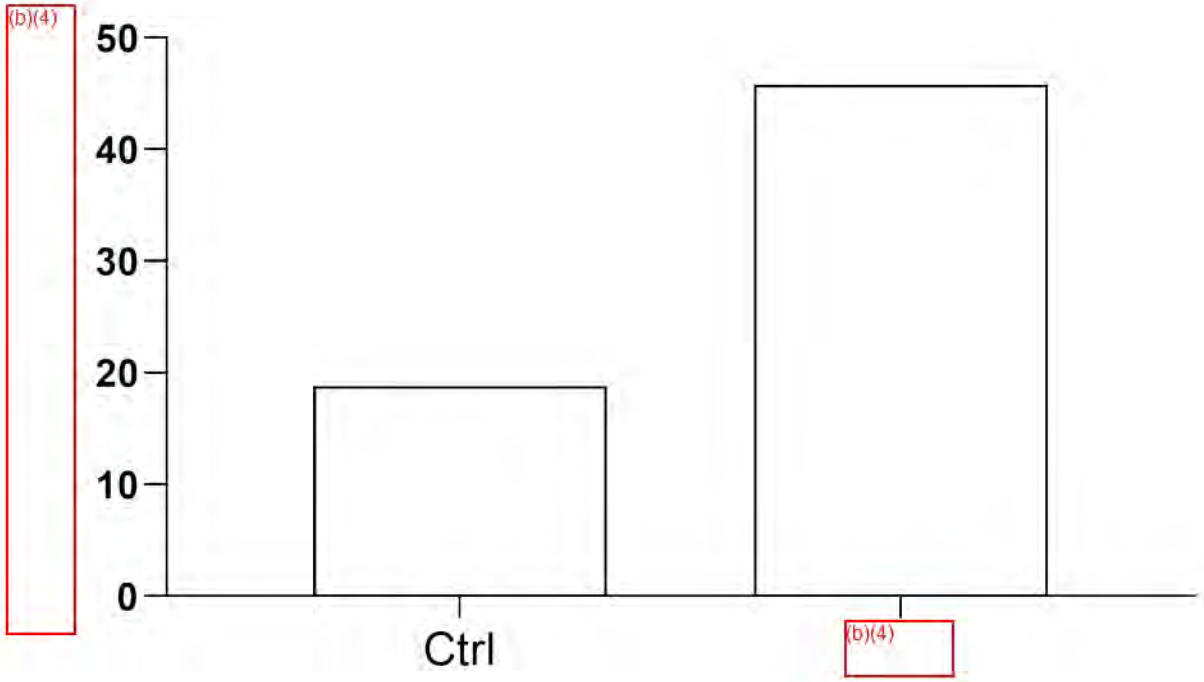


Figure 1. (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1683

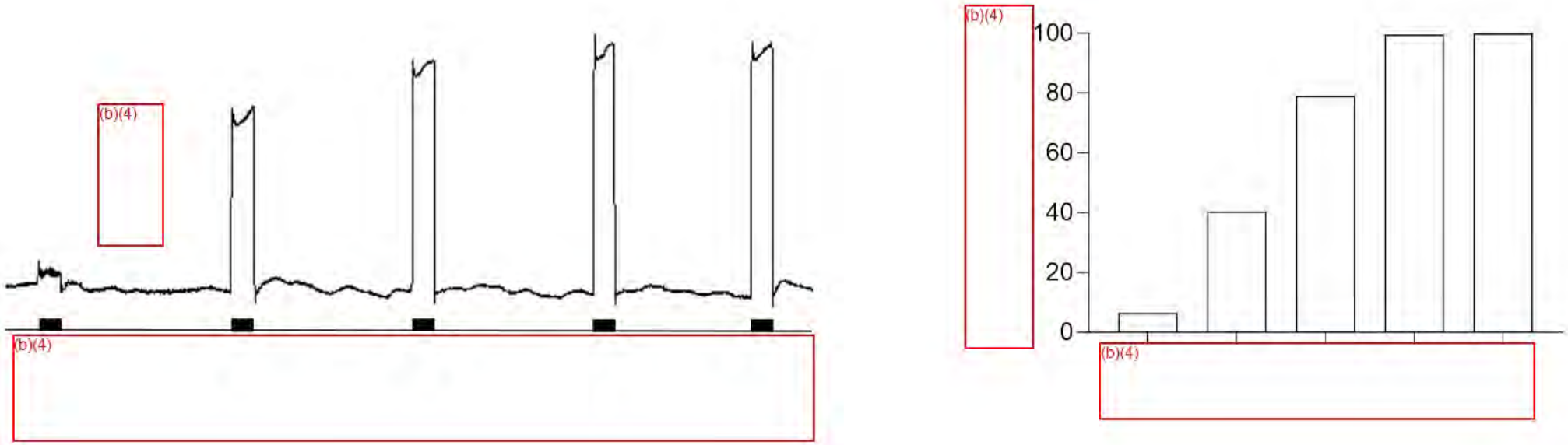


Figure 2. (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1684

Task 1.2.3 (b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

Task 1.2.3 Restore Sexual Function – Vaginal Contraction

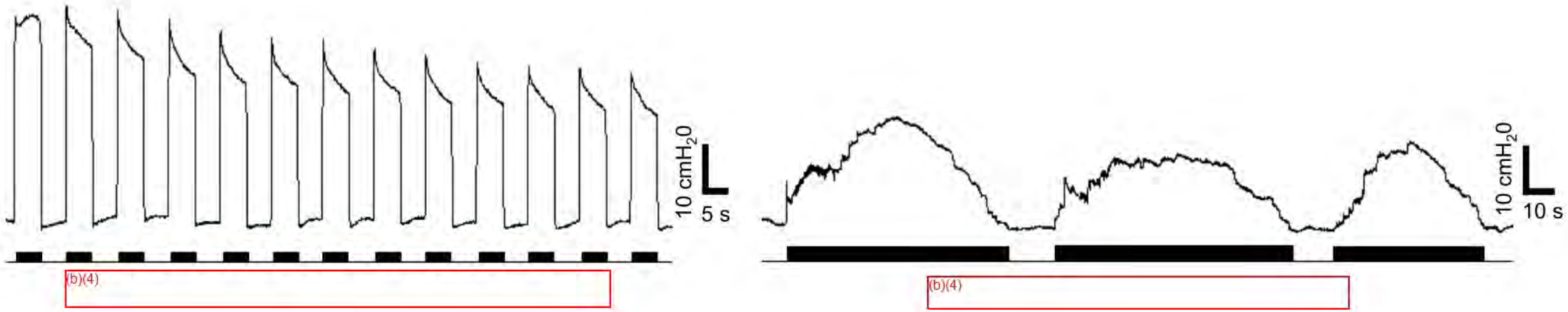


Figure 4. (b)(4)

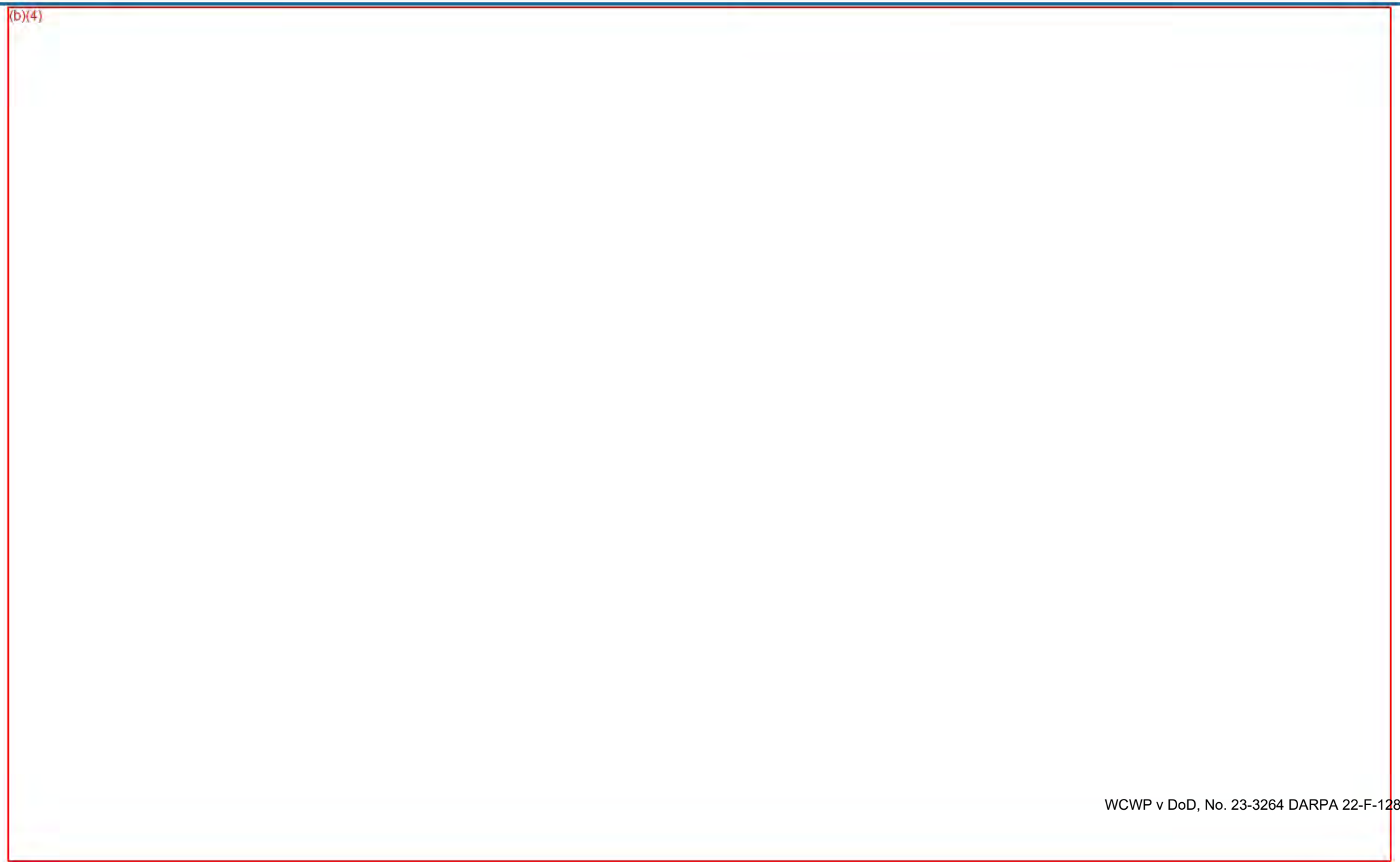
(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1686

(b)(4)

Figure 5

(b)(4)



(b)(4)

Figure 6

(b)(4)

(b)(4)

Figure 7

(b)(4)

(b)(4)

Figure 8

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1690

Task 1.16: FDA IDE submission (b)(4)

(b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.3: Restore sexual function (b)(4)
  Restoring female sexual function in 2 cats by (b)(4) stimulation
- Task 1.4: Implantable pulse generator (b)(4)
  Integrate pulse generator circuit into can (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.6: Implantable pulse generator (b)(4)
  System verification completed (b)(4)
  Documentation Supporting the IDE submission (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.8: Physician/Investigator controller (b)(4)
  Evaluation board fabricated/assembled and initial evaluation complete (b)(4)
  Integration with a simple enclosure with display and firmware (b)(4)
  Final documentation to support the FDA IDE (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1692

Work Plan for Next 4 Weeks (b)(4)

- Task 1.9: Patient controller (b)(4)

  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)

  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 1.11: GLP animal study (b)(4)

  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)

  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)

  Continue to prepare IDE application (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1693

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [1/1/2022] – [1/31/2022]

1/31/2022

Overview – Technical Update

- Sexual function study was performed in 2 female cats to induce vaginal contraction and secretion.
- The (b)(4) schematic was shrunken down to fit into the (b)(4) can. (b)(4)
  (b)(4)
- Labels were created for the IDE (b)(4)
- The electrical and mechanical testing of (b)(4) All testing/validation documentations required for the FDA IDE submission were completed.
- The IFU was written and completed by Med-Ally and Thermaquil for FDA IDE submission.
- The (b)(4) is under development.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested.
  (b)(4)
  - (b)(4) is being investigated to replace some (b)(4)
    - (b)(4) has both (b)(4) capabilities on site.
  - (b)(4) was delivered to Med-Ally for (b)(4) construction.
  - (b)(4) was delivered to Med-Ally for (b)(4) construction.
- The FDA IDE submission is fully drafted and is now under regulatory review for final submission.

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1698

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.3: Restore sexual function [redacted]
  - Restoring female sexual function in 2 cats by pudendal nerve stimulation – [redacted]
- Task 1.4: Implantable pulse generator [redacted]
  - Integrate pulse generator circuit into can [redacted]
  - Full integration and test completed for initial prototype [redacted]
- Task 1.6: External pulse generator [redacted]
  - System verification completed [redacted]
  - Documentation Supporting the IDE submission [redacted]
- Task 1.7: [redacted] electrodes for human use [redacted]
  - First prototypes of [redacted] delivered for test [redacted]
  - Finalize design and [redacted] production [redacted]
  - Biocompatibility test is completed. Documentations for FDA IDE submission [redacted]
- Task 1.8: Physician/Investigator controller [redacted]
  - Evaluation board fabricated/assembled and initial evaluation complete [redacted]
  - Integration with a simple enclosure with display and firmware [redacted]
  - Final documentation to support the FDA IDE [redacted]

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4 Week Work Plan from Previous Report

- Task 1.9: Patient controller (b)(4)
  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporating feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  Continue to prepare IDE application (b)(4)

COVID related updates

- Current MSR period – (b)(4) (1/1/2022-1/31/2022)
  - (b)(4)

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Big Wins – (b)(4) FDA IDE Approval

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1704

Big Wins – The Physician Controller GUI

(b)(4)

Figure 2. The physician controller GUI for wireless control (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1705

Big Wins – Labeling and Package (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1706

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 1/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.3 Restore sexual function (b)(4) (b)(4)	(b)(4)					Milestone 1.2.3(1-4) – Deliverable 1.2.3	
1.4 Implantable pulse generator (b)(4)							
1.4.3 Integrate pulse generator circuit into can (b)(4)	(b)(4)					Milestone 1.4.3 – Deliverable 1.4	
1.4.5 Full integration and test completed for initial prototype (b)(4)						Milestone 1.4.5 – Deliverable 1.4	
1.6 External pulse generator (b)(4)							
1.6.3 System verification completed (b)(4)	(b)(4)					Milestone 1.6.3 – Deliverable 1.6.1 – Deliverable 1.6.2	
1.6.4 Documentation Supporting the IDE submission (b)(4)						Milestone 1.6.4 – Deliverable 1.6.1	
1.7 (b)(4) electrodes for human use (b)(4)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1707

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4)

Date: 1/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.8 Physician/Investigator controller (b)(4)							(b)(4)
1.8.2 Evaluation board fabricated/assembled and initial evaluation complete (b)(4)	(b)(4)					Milestone 1.8.1	
1.8.3 Integration with a simple enclosure with display and firmware (b)(4)						Milestone 1.8.1	
1.8.4 Final documentation to support the FDA IDE as an accessory device (b)(4)						Milestone 1.8.4 – Deliverable 1.8	
1.9 Patient controller (b)(4)							
1.9.2 Verification testing completed (b)(4)	(b)(4)					Milestone 1.9.2 – Deliverable 1.9	
1.10 Software Development Kit (SDK) (b)(4)							
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
1.16 FDA IDE Submission (b)(4)							
1.16.1 FDA IDE application for the (b)(4) is submitted	(b)(4)					Milestone 1.16 – Deliverable 1.16	
1.13 Early feasibility human clinical protocol (b)(4)							
1.13 Early feasibility human clinical protoco (b)(4)	(b)(4)					Milestone 1.13 – Deliverable 1.13	
1.11 GLP animal study (b)(4)							
1.11 GLP animal study						Milestone 1.11 – Deliverable 1.11	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1708

Technical Progress Summary

- (b)(4) stimulation successfully induced (b)(4) and improved (b)(4) by increasing secretion in 3 female cats. (b)(4) are the most effective stimulation frequencies.
- The (b)(4) schematic was shrunken down to fit into the (b)(4) can. (b)(4) (b)(4)
- Labels were created for the IDE (b)(4)
- The electrical and mechanical testing of (b)(4) have been completed. All testing/validation documentations required for the FDA IDE submission were completed.
- The IFU was written and completed by Med-Ally and Thermaquil for FDA IDE submission.
- The (b)(4) is under development.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
- The FDA IDE submission is fully drafted and under review by regulatory expert (b)(4); (b)(6)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1709

Task 1.2.3 (b)(4)

Figure 4. (b)(4)

(b)(4)

Task 1.2.3 (b)(4)

(b)(4)

Figure 5. (b)(4)

(b)(4)

Task 1.2.3 (b)(4)

(b)(4)

(b)(4)

Task 1.2.3 Restore Sexual Function – Vaginal Contraction

(b)(4)

Figure 7. (b)(4)

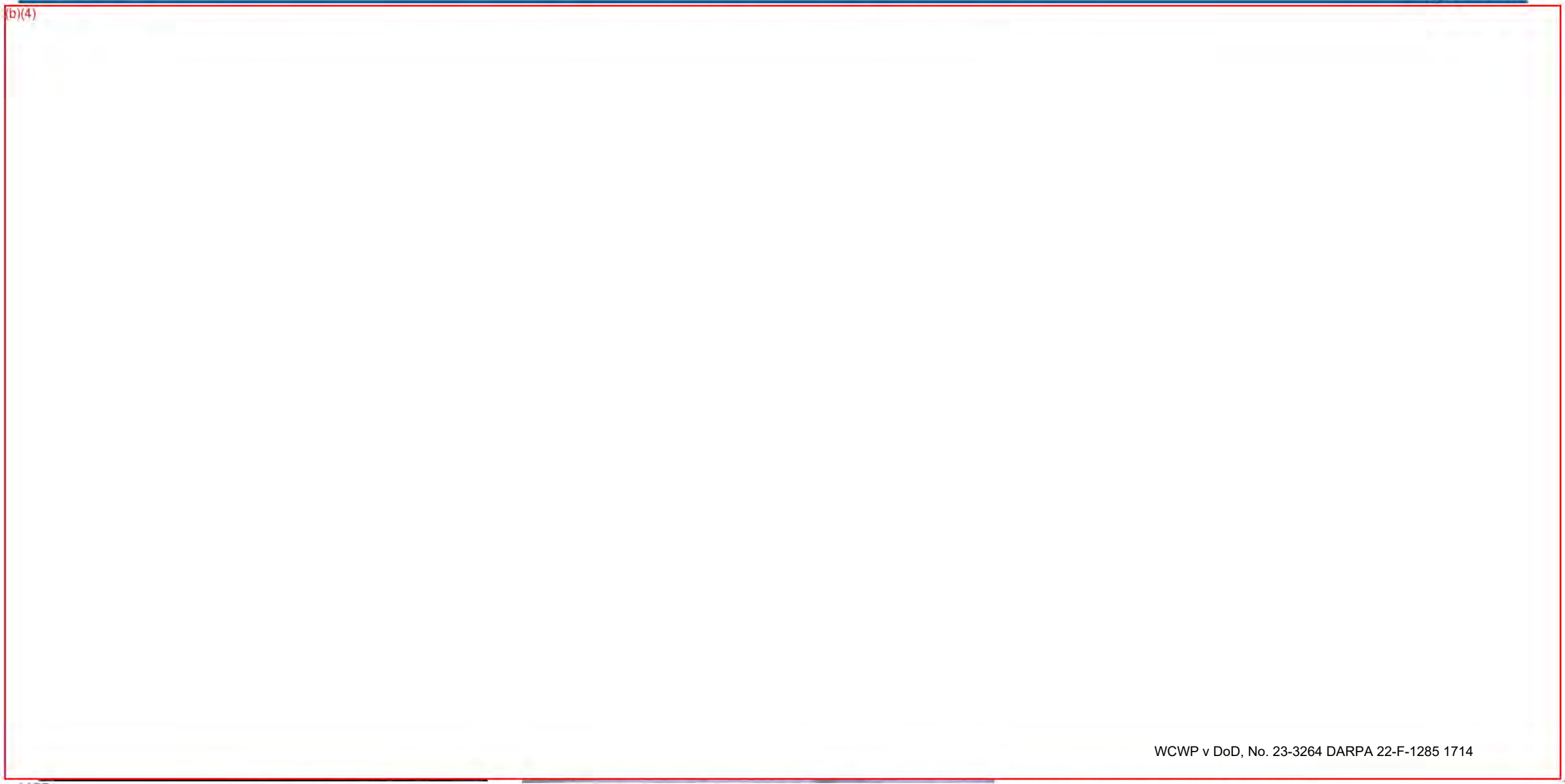
(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1713

(b)(4) manufacturing process under qualifications

Figure 8

(b)(4)

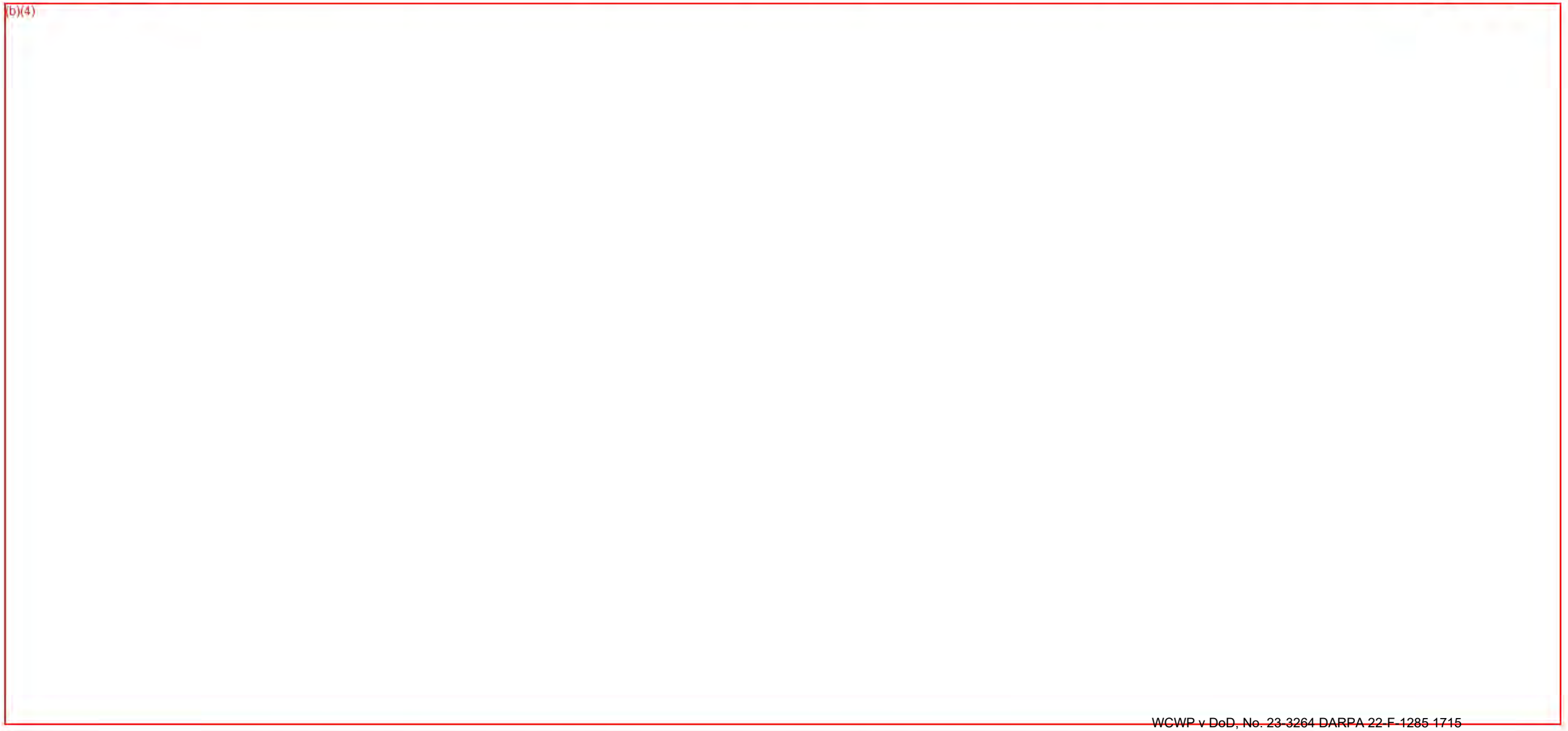


WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1714

(b)(4) manufacturing process under qualifications (continued)

Figure 9

(b)(4)



WCWP v DoD, No. 23-3264 DARPA-22-F-1285-1715

(b)(4)

Figure 10

(b)(4)

(b)(4) Internal Electrical Design

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

Task 1.16: FDA IDE submission for (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1720

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.3: Restore sexual function (b)(4)

  Restoring female sexual function in 1-2 cats and summarize the results.
- Task 1.4: Implantable pulse generator (b)(4)

  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)

  First prototypes of (b)(4) delivered for test (b)(4)

  Finalize design and (b)(4) production (b)(4)

  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.9: Patient controller (b)(4)

  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)

  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1721

Work Plan for Next 4 Weeks (b)(4)

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporated feedback from FDA (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  IDE application is completely drafted and being reviewed by regulatory expert (b)(4); (b)(6)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1722

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [2/1/2022] – [2/28/2022]

2/28/2022

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1726

Overview – Technical Update

- Sexual function study was completed in 4 female cats to (b)(4) (b)(4) The data were analyzed, and the manuscript (attached) is ready for submission after DARPA review.
- (b)(4) circuit board layout underway
- The (b)(4) is under development.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
  - (b)(4) is being investigated to replace (b)(4) processes.
    - Med-Ally has both (b)(4) capabilities on site.
  - (b)(4) were delivered on site to Med-Ally (b)(4)
- (b)(4) configurations for (b)(4) implantation study are being revisited and analyzed
- The FDA IDE submission was completed. FDA received the submission on (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1727

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.3: Restore sexual function (b)(4)
  Restoring female sexual function in 1-2 cats and summarize the results – (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.9: Patient controller (b)(4)
  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1730

4 Week Work Plan from Previous Report

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporated feedback from FDA into our IDE – (b)(4)
- Task 1.16: FDA IDE submission (b)(4)
  IDE application has been submitted to FDA, pending FDA approval

COVID related updates

- Current MSR period – (b)(4) (2/1/2022-2/28/2022)
  - (b)(4)

Big Wins – FDA IDE Submission

Figure 1. FDA acknowledgment letter that the IDE submission was received (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1733

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 2/28/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.3 Restore sexual function (b)(4) (b)(4)		(b)(4)				Milestone 1.2.3(1-4) – Deliverable 1.2.3	
1.4 Implantable pulse generator with (b)(4)							
1.4.5 Full integration and test completed for initial prototype (b)(4)		(b)(4)				Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) **electrodes for** (b)(4)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)		(b)(4)				Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1734

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 2/28/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.9 Patient controller (b)(4)							(b)(4)
1.9.2 Verification testing completed (b)(4)	(b)(4)					Milestone 1.9.2 – Deliverable 1.9	
1.10 Software Development Kit (SDK) (b)(4)							
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
1.16 FDA IDE Submission (b)(4)							
1.16.1 FDA IDE application for the (b)(4) is submitted	(b)(4)					Milestone 1.16 – Deliverable 1.16	
1.16.2 FDA IDE approval for the (b)(4)						Milestone 1.16.2 – Deliverable 1.16.2	
1.13 Early feasibility human clinical protocol (b)(4)							
1.13 Early feasibility human clinical protocol (b)(4)	(b)(4)					Milestone 1.13 – Deliverable 1.13	
1.11 GLP animal study (b)(4)							
1.11 GLP animal study						Milestone 1.11 – Deliverable 1.11	

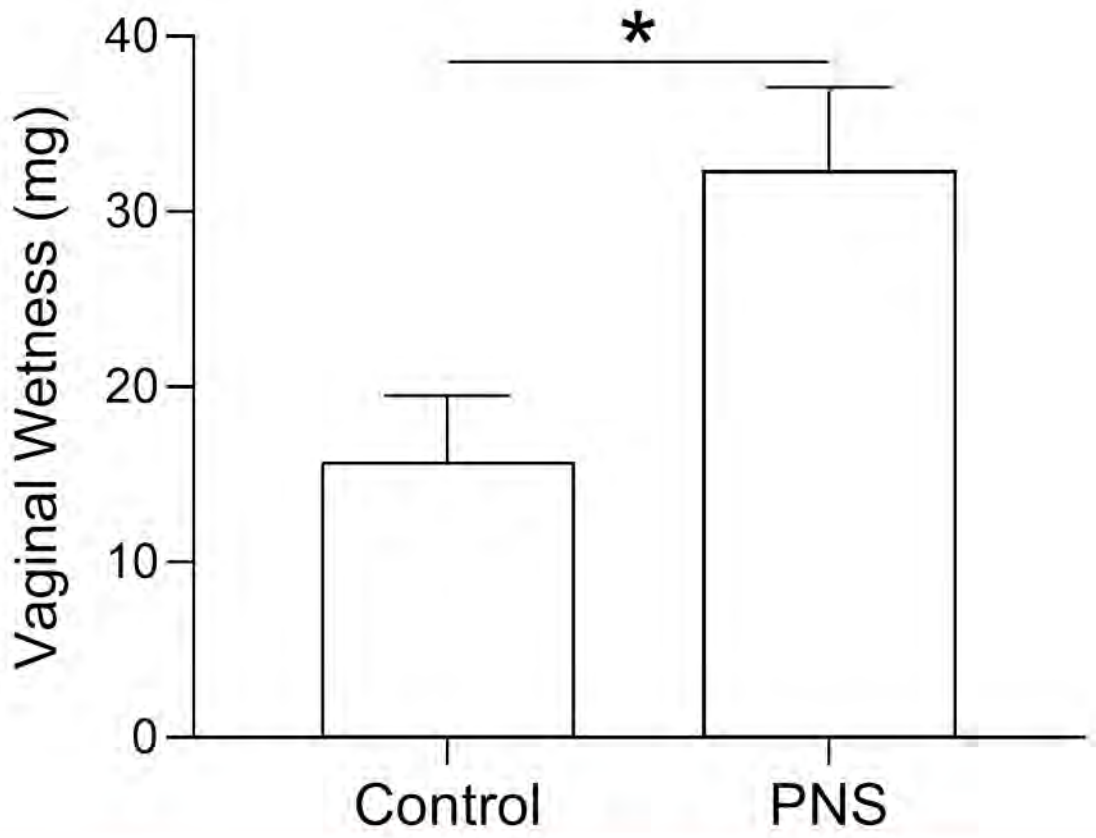
WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1735

Technical Progress Summary

- (b)(4) stimulation at (b)(4) is effective in inducing vaginal contraction and increasing vaginal wetness. A manuscript is written and ready for submission after DARPA review.
- (b)(4) circuit board layout underway
- The (b)(4) is under development.
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
  - (b)(4) is being investigated to replace (b)(4) processes.
    - (b)(4) has both (b)(4) capabilities on site.
  - (b)(4) Electrodes were delivered on site to (b)(4)
- (b)(4)
- Our IDE was submitted to FDA. (b)(4)
(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1736

Task 1.2.3 Restore Sexual Function - Vaginal Wetness



(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1737

Task 1.2.3

(b)(4)

(b)(4)

P

Task 1.2.3 (b)(4)

(b)(4)

Task 1.2.3 Restore Sexual Function – Vaginal Contraction

(b)(4)

Figure 5. (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1740

(b)(4)

(b)(4)

Task 1.16: FDA IDE submission for (b)(4)

(b)(4); (b)(6)

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.4: Measure fullness of bladder and bowel (b)(4)
  Recording activity from pudendal nerve or sacral roots to detect bladder or colon fullness in 2 cats.
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.9: Patient controller (b)(4)
  Verification testing completed (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporated feedback from FDA into the IDE, pending FDA approval
- Task 1.16: FDA IDE submission (b)(4)
  IDE application is being reviewed by FDA

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1744

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- (b)(4)

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [3/1/2022] – [3/31/2022]

3/31/2022

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1748

Overview – Technical Update

- Bladder and bowel fullness are evaluated by recording nerve activity from the (b)(4) or (b)(4) in 2 cats.
- (b)(4) The original components were identified and sourced appropriately. (b)(4)
  (b)(4)
- (b)(4)
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
- (b)(4) configurations for the (b)(4) are revisited and analyzed
- We responded to (b)(4) interactive requests from FDA (b)(4)
- IDE was unconditionally approved by FDA (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1749

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.
- (b)(4)

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.4: Measure fullness of bladder and bowel (b)(4)

  Recording nerve activity from (b)(4) to evaluate bladder and bowel fullness – (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)

  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)

  First prototypes of (b)(4) delivered for test (b)(4)

  Finalize design and (b)(4) production (b)(4)

  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)

  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)

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4 Week Work Plan from Previous Report

- Task 1.11: GLP animal study (b)(4)
  (b)(4)
- Task 1.13: Early feasibility human clinical protocol (b)(4)
  Incorporated feedback from FDA (b)(4) into IDE
- Task 1.16: FDA IDE submission (b)(4)
  IDE has been approved

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COVID related updates

- Current MSR period – (b)(4) (3/1/2022-3/31/2022)
  - (b)(4)

Big Wins – FDA IDE Approval

(b)(4)

(b)(4); (b)(6)

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Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 3/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.4 Measure fullness of bladder and bowel (b)(4)	(b)(4)					Milestone 1.2.4(1-3) – Deliverable 1.2.4	
1.4 Implantable pulse generator (b)(4)							
1.4.5 Full integration and test completed for initial prototype (b)(4)	(b)(4)				(b)(4)	Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) electrodes for human use (MAC4 to MAC15)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

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Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 2/28/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.9 Patient controller (b)(4)							(b)(4)
1.9.2 Verification testing completed (b)(4)	(b)(4)					Milestone 1.9.2 – Deliverable 1.9	
1.10 Software Development Kit (SDK) (b)(4)							
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
1.16 FDA IDE Submission (b)(4)							
1.16.2 FDA IDE approval for the (b)(4)	(b)(4)					Milestone 1.16.2 – Deliverable 1.16.2	
1.13 Early feasibility human clinical protocol (b)(4)							
1.13 Early feasibility human clinical protocol (b)(4)	(b)(4)					Milestone 1.13 – Deliverable 1.13	
1.11 GLP animal study (b)(4)							
1.11 GLP animal study						Milestone 1.11 – Deliverable 1.11	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1757

Technical Progress Summary

- (b)(4)
- The (b)(4) circuit is (b)(4)
- The (b)(4) is being fabricated
- The complete (b)(4) manufacturing process continues to be improved upon, inspected and tested. (b)(4) assembly is the focus right now.
- (b)(4) configurations for the (b)(4) are revisited and analyzed
- We responded to (b)(4) interactive requests (b)(4) from FDA within the FDA's suggested response times
- Our IDE was approved unconditionally (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1758

Task 1.2.4 Measure fullness of bladder and bowel – experimental setup

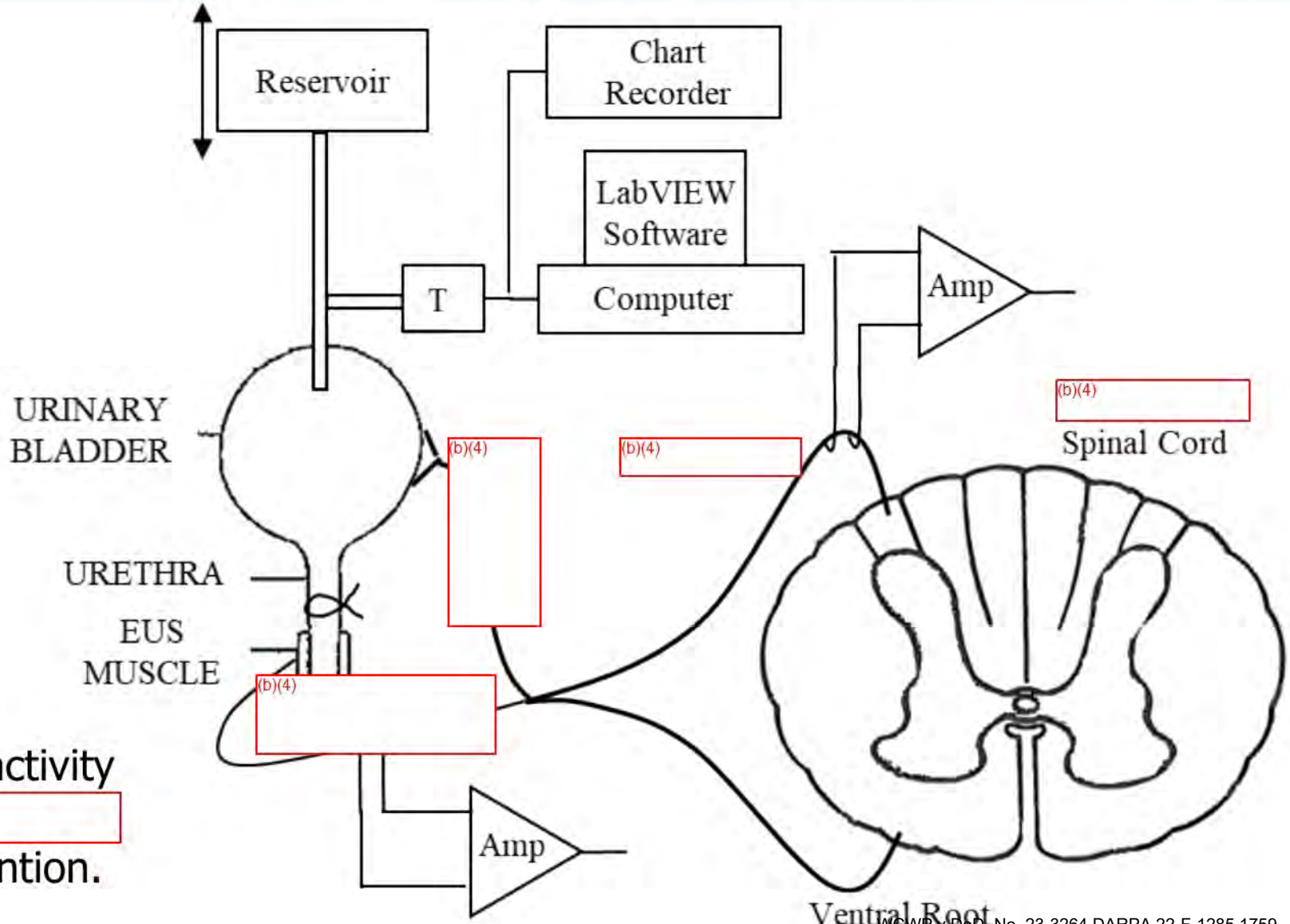

Fig.1. Recording nerve activity from (b)(4) (b)(4) during bladder distention.

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1759

Task 1.2.4 Measure fullness of bladder and bowel – pudendal nerve

Task 1.2.4 Measure fullness of bladder and bowel – sacral dorsal roots

(b)(

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1761

(b)(4)

(b)(4)

Modified (b)(4) Process for (b)(4)

(b)(4)

(b)(4) Process for (b)(4)

(b)(4)

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Task 1.16: FDA IDE submission (b)(4)

(b)(4); (b)(6)

Task 1.16: FDA IDE submission (b)(4)

(b)(4); (b)(6)

Task 1.16: FDA IDE submission for (b)(4)

(b)(4); (b)(6)

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Task 1.16: FDA IDE submission for (b)(4)

(b)(4); (b)(6)

Task 1.16: FDA IDE submission for (b)(4)

(b)(4); (b)(6)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1769

Task 1.16: FDA IDE submission (b)(4)

(b)(4); (b)(6)

Fig.12. FDA letter thanking our quick and comprehensive responses to interactive requests

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1770

Work Plan for Next 4 Weeks (b)(4)

- Task 1.2.4: Measure fullness of bladder and bowel (b)(4)

  Recording activity from (b)(4) to detect bladder or colon fullness in 2 cats.
- Task 1.4: Implantable pulse generator (b)(4)

  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)

  First prototypes of (b)(4) delivered for test (b)(4)

  Finalize design and (b)(4) production (b)(4)

  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)

  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)

  Preparing to submit IRB protocols for human studies at University of Pittsburgh (b)(4)

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- (b)(4)

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4), (b)(6)

Reporting Period: [4/1/2022] – [4/30/2022]

4/30/2022

Overview – Technical Update

- Bladder and bowel fullness are evaluated by recording nerve activity from the (b)(4) (b)(4) in 2 cats.
- Human study protocol was submitted to University of Pittsburgh IRB for approval.
- The (b)(4) circuit layout is complete. Currently reaching out to multiple companies to fabricate the (b)(4) board. (b)(4) (b)(4)
- The (b)(4) has been finalized. First prototype of (b)(4) are being created to be tested in cat study.
- The biocompatibility evaluation plan is in process and should be completed by (b)(4) Currently, information for the (b)(4) is being delivered to create the evaluation plan.
- Began drafting early feasibility study protocol (b)(4) (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1776

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.
- (b)(4) was received.

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1777

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 1.2.4: Measure fullness of bladder and bowel [(b)(4)]
  Recording nerve activity from [(b)(4)] roots to evaluate bladder and bowel fullness – [(b)(4)]
- Task 2.2: IRB approval and NIWC HRPO approval for human studies [(b)(4)]
  IRB protocol approval for human studies at University of Pittsburgh [(b)(4)]
- Task 1.4: Implantable pulse generator [(b)(4)]
  Full integration and test completed for initial prototype [(b)(4)]
- Task 1.7: [(b)(4)] electrodes for human use [(b)(4)]
  First prototypes of [(b)(4)] delivered for test [(b)(4)]
  Finalize design and [(b)(4)] production [(b)(4)]
  Biocompatibility test is completed. Documentations for FDA IDE submission [(b)(4)]
- Task 1.10: Software Development Kit (SDK) [(b)(4)]
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API [(b)(4)]

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1779

COVID related updates

- Current MSR period – (b)(4) (4/1/2022-4/30/2022)
  - (b)(4)

Big Wins –

- Nothing to Report

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4)

Date: 4/30/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.2 Animal studies to develop the external system and the implantable system (b)(4)							(b)(4)
1.2.4 Measure fullness of bladder and bowel (b)(4)	(b)(4)					Milestone 1.2.4(1-3) – Deliverable 1.2.4	
2.2 IRB approval and NIWC HRPO approval for human studies (b)(4)							
2.2.1 Prepare and submit IRB protocols for human studies	(b)(4)						
1.4 Implantable pulse generator (b)(4)							
1.4.5 Full integration and test completed for initial prototype (b)(4)	(b)(4)					Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) **electrodes for human use** (b)(4)							
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1782

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 4/30/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.10 Software Development Kit (SDK)	(b)(4)						(b)(4)
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
2.11 Early feasibility human clinical protocol	(b)(4)						
2.11 Early feasibility human clinical protocol (b)(4)	(b)(4)					Milestone 2.11 – Deliverable 2.11.1	
2.12 FDA IDE (b)(4)							
2.12.1 FDA IDE (b)(4) for (b)(4)	(b)(4)					Milestone 2.13 – Deliverable 2.13.1	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1783

Technical Progress Summary

- (b)(4)
- Working with University of Pittsburgh IRB for human study protocol approval
- The (b)(4) layout is complete. Currently reaching out to multiple companies to fabricate the (b)(4) board. (b)(4)
  (b)(4)
- First prototype of (b)(4) are being created to be tested in cat study.
- The biocompatibility evaluation plan is in process and should be completed (b)(4)
- Began drafting early feasibility study protocol and (b)(4)

Task 1.2.4 Measure fullness of bladder and bowel – experimental setup

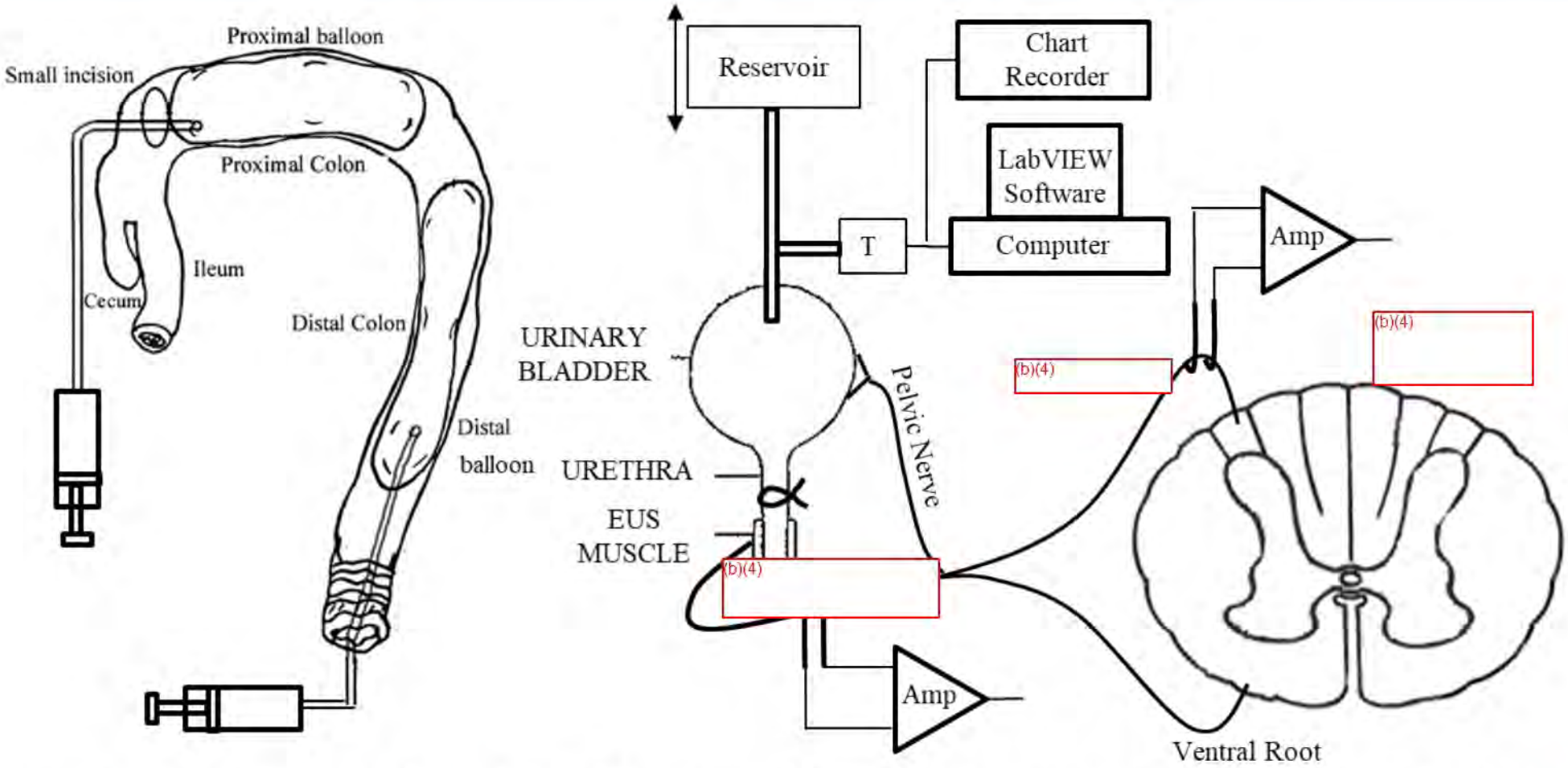

Fig.1. Experimental setup to detect bladder/bowel fullness by recording nerve activity from (b)(4) (b)(4) Bladder is distended by raising a saline reservoir and colon is distended by infusing saline into the colon balloons. (b)(4) is used to record nerve activity.

Task 1.2.4 Measure fullness of bladder and bowel – (b)(4)

(b

Task 1.2.4 Measure fullness of bladder and bowel – S3 Dorsal Root

(b)(4)

Task 1.2.4 Measure fullness of bladder and bowel – (b)(4)

(b)(4)

Task 2.2 Clinical Study IRB Approval

(b)(4)

(b)(4)

(b)(4)

(b)(4) Prototypes of (b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1791

(b)(4) design

(b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 2.2: IRB approval and NIWC HRPO approval for human studies using the external stimulation system
  Obtaining IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to Report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [5/1/2022] – [5/31/2022]

5/31/2022

Overview – Technical Update

- Human study protocol was submitted to University of Pittsburgh IRB for approval. We have received (b)(4) of comments/questions from IRB and responded accordingly.
- The (b)(4) circuit board is complete. Part placement is complete with routing (b)(4)
- (b)(4)
- First prototype of (b)(4) are being created to be sent to be verified in cat study. Currently, (b)(4)
- The biocompatibility evaluation plan was written and is being reviewed by an expert.
- Continued drafting early feasibility study protocol (b)(4) for inclusion in (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1798

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.
- (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1799

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 1.10: Software Development Kit (SDK) (b)(4)
  At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1801

COVID related updates

- Current MSR period – (b)(4) (5/1/2022-5/31/2022)
  - (b)(4)

Big Wins –

- Nothing to Report

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 5/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
2.2 IRB approval and NIWC HRPO approval for human studies		(b)(4)					(b)(4)
2.2.1 Prepare and submit IRB protocols for human studies		(b)(4)					
1.4 Implantable pulse generator with		(b)(4)					
1.4.5 Full integration and test completed for initial prototype (b)(4)		(b)(4)				Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) electrodes for human use		(b)(4)					
1.7.3 First prototypes of (b)(4) delivered for test (b)(4)		(b)(4)				Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1804

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4)

Date: 5/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.10 Software Development Kit (SDK)	(b)(4)						(b)(4)
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)				(b)(4)	Milestone 1.10.2 – Deliverable 1.10	
2.11 Early feasibility human clinical protocol	(b)(4)						
2.11 Early feasibility human clinical protocol (b)(4)	(b)(4)					Milestone 2.11 – Deliverable 2.11.1	
2.12 FDA IDE (b)(4)							
2.12.1 FDA IDE (b)(4) (b)(4)	(b)(4)					Milestone 2.13 – Deliverable 2.13.1	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1805

Technical Progress Summary

- Working with University of Pittsburgh IRB for human study protocol approval. Responded (b)(4) of comments/questions from IRB.
- The (b)(4) circuit board is complete. There are multiple companies currently searching for all the parts needed to make the (b)(4)
- (b)(4)
- The biocompatibility evaluation plan was written and is being reviewed by an expert.
- Continued drafting early feasibility study protocol (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1806

Task 2.2 Clinical Study IRB Approval

(b)(4); (b)(6)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

First Prototypes of (b)(4)

(b)(4)

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Figure 5: Flow Diagram (b)(4)

(b)(4)

(b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  Obtaining IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol for IPG system
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA (b)(4)

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to Report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [6/1/2022] – [6/30/2022]

6/30/2022

Overview – Technical Update

- (b)(4)
- The third paper for restoring male sexual function is now accepted for publication on Neuromodulation: Technology at Neural Interface.
- (b)(4)
- (b)(4) are in the process of being populated and are scheduled to be delivered (b)(4)
- (b)(4) is updated to be more intelligent independent of GUI commands.
- (b)(4)

  (b)(4) Minor adjustments will be made in (b)(4) and then re-printed.
- (b)(4)
-

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1817

Overview – Technical Update

- The (b)(4) has started development. This (b)(4) will be a minor adjustment from (b)(4)
- (b)(4) scheduled to be delivered on (b)(4)
- (b)(4)
- The biological/biocompatibility evaluation was further refined.
- Continued drafting early feasibility study protocol (b)(4) (b)(4)
- (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1818

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.
- The contract amendment with (b)(4) is signed for additional funding, (b)(4)
(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1819

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1821

COVID related updates

- Current MSR period – (b)(4) (6/1/2022-6/30/2022)
  - (b)(4)

Big Wins – The 3rd study of male sexual function is published

Neuromodulation: Technology at the Neural Interface <em@editorialmanager.com>

(b)(4)

To: (b)(6)@pitt.edu>

Manuscript Number: NEUROM-D-22-00211R1

Penile Erection Induced by Stimulation of Sacral S1/S2 Spinal Root in Cats

Dear (b)(6)

Thank you for submitting your manuscript to Neuromodulation: Technology at the Neural Interface.

I am pleased to inform you that your manuscript has been accepted for publication.

We look forward to your continued participation in our journal, and we hope you will consider us again for future submissions.

Kind regards,

(b)(6)

Neuromodulation: Technology at the Neural Interface

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1823

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 6/30/2022

SOW Task #		Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
2.2	**IRB approval and NIWC HRPO approval for human studies** (b)(4)							(b)(4)
2.2.1	Prepare and submit IRB protocols for human studies	(b)(4)				(b)(4)	Milestone 2.2.1 – Deliverable 2.2.1	
2.2.2	Protocol review completed by NIWC HRPO						Milestone 2.2.2 – Deliverable 2.2.2	
1.4	**Implantable pulse generator** (b)(4)							
1.4.5	Full integration and test completed for initial prototype (b)(4)	(b)(4)					Milestone 1.4.5 – Deliverable 1.4	
1.7	(b)(4) **electrodes for human use** (b)(4)							
1.7.3	First prototypes of (b)(4) delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4	Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5	Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1824

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4)

Date: 6/30/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.10 Software Development Kit (SDK)	(b)(4)						(b)(4)
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)				(b)(4)	Milestone 1.10.2 – Deliverable 1.10	
2.10 (b)(4)							
2.10 (b)(4)						Milestone 2.10 – Deliverable 2.10.1	
2.11 Early feasibility human clinical protocol (b)(4)							
2.11 Early feasibility human clinical protocol for (b)(4)	(b)(4)					Milestone 2.11 – Deliverable 2.11.1	
2.12 FDA IDE (b)(4)							
2.12.1 FDA IDE (b)(4) (b)(4)	(b)(4)					Milestone 2.13 – Deliverable 2.13.1	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1825

Technical Progress Summary

- (b)(4)
- Third study of restoring male sexual function is published.
- The number of remaining components to purchase (b)(4)
- (b)(4)
- (b)(4)
- The (b)(4) is also updated.
- The (b)(4) are in development.
- (b)(4)
- The (b)(4) finished (b)(4)
- The biological/biocompatibility evaluation was further refined.
- Continued drafting (b)(4)
- (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1826

Task 2.2 Clinical Study IRB Approval

(b)(4), (b)(6)

(b)(4) of the most up to date (b)(4)

(b)(4)

(b)(4) has approved (b)(4)

(b)(4)

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(b)(4)

(b)(4)

(b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1831

Work Plan for Next 4 Weeks (b)(4)

- Task 2.2: IRB approval and NIWC HRPO approval for human studies using the (b)(4)
  Obtaining IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1832

Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to Report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [7/1/2022] – [7/31/2022]

7/31/2022

Overview – Technical Update

- We have identified the external IRB (WCG IRB) (b)(4)
  (b)(4)
- The fourth paper for restoring female sexual function is now accepted for publication on Journal of Sexual Medicine (Final version of the manuscript is attached).
- All remaining (b)(4) were found (b)(4)
  (b)(4)
- All electrical and mechanical components for the (b)(4) PCBs are in the process of being populated and the firmware will be tested (b)(4)
- The (b)(4) is being updated to be more independent of GUI commands.
- (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1837

Overview – Technical Update

- The biological evaluation plan has been defined, (b)(4)
(b)(4)
- Many of the surgical tools (b)(4)
- Continued drafting early feasibility study protocol (b)(4)
(b)(4)
-

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1838

Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: Implantable pulse generator (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  First prototypes of (b)(4) delivered for test (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1841

COVID related updates

- Current MSR period – (b)(4) (7/1/2022-7/31/2022)
  - (b)(4)

Big Wins – The 4th study of female sexual function is published

Journal of Sexual Medicine - Decision on Manuscript JSM-22-200.R1

Journal of Sexual Medicine <onbehalfof@manuscriptcentral.com>

(b)(4)

To: (b)(6)@mail2.sysu.edu.cn (b)(6)@mail2.sysu.edu.cn>; (b)(6)@outlook.com>, (b)(6)@pitt.edu>; (b)(6)
Bing (b)(6)@pitt.edu> (b)(6)@pitt.edu>; (b)(6)@pitt.edu>; (b)(6)
(b)(6)@pitt.edu>; (b)(6)@upmc.edu (b)(6)@upmc.edu>; (b)(6)@pitt.edu>

Cc: (b)(6)@gmail.com (b)(6)@gmail.com>, (b)(6)@unifi.it (b)(6)@unifi.it>; (b)(6)@gmail.com
(b)(6)@gmail.com>

(b)(4)

Dear (b)(6)

congratulations!!!!!It is a pleasure to accept your manuscript entitled "Vaginal Lubrication and Pressure Increase Induced by Pudendal Nerve Stimulation in Cats" in its current form for publication in the Journal of Sexual Medicine. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

(b)(6)

(b)(6)@gmail.com

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1843

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 7/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
2.2 IRB approval and NIWC HRPO approval for human studies (b)(4)							(b)(4)
2.2.1 Prepare and submit IRB protocols for human studies	(b)(4)					Milestone 2.2.1 – Deliverable 2.2.1	
2.2.2 Protocol review completed by NIWC HRPO						Milestone 2.2.2 – Deliverable 2.2.2	
1.4 Implantable pulse generator (b)(4)							
1.4.5 Full integration and test completed for initial prototype (b)(4)	(b)(4)					Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) **electrodes for human use** (b)(4)							
1.7.3 First prototypes of leads delivered for test (b)(4)	(b)(4)					Milestone 1.7.3 – Deliverable 1.7	
1.7.4 Finalize design and (b)(4) production (b)(4)						Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (b)(4)						Milestone 1.7.5 – Deliverable 1.7	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1844

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4)

Date: 7/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
1.10 Software Development Kit (SDK)	(b)(4)						(b)(4)
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
2.10 (b)(4)							
2.10 (b)(4)	(b)(4)					Milestone 2.10 – Deliverable 2.10.1	
2.11 Early feasibility human clinical protocol	(b)(4)						
2.11 Early feasibility human clinical protocol for (b)(4)	(b)(4)					Milestone 2.11 – Deliverable 2.11.1	
2.12 FDA IDE (b)(4)							
2.12.1 FDA IDE (b)(4) (b)(4)	(b)(4)					Milestone 2.13 – Deliverable 2.13.1	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1845

Technical Progress Summary

- The external IRB (b)(4) are identified and approved by University COI committee. (b)(4) and preparing IRB submission.
- Fourth study of restoring female sexual function is published.
- All remaining (b)(4) components were found (b)(4)
- (b)(4) will populated, and the firmware will be tested (b)(4)
- (b)(4) have been tested, and the programs are in development.
- First prototype of (b)(4) is delivered for testing at University of Pittsburgh.
- (b)(4)
-
- The biological evaluation plan has been defined, (b)(4) (b)(4)
- Continued drafting early feasibility study protocol and (b)(4)
- (b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1846

Task 2.2 Clinical Study IRB Approval

(b)(4)

MASTER CLINICAL RESEARCH SERVICES AGREEMENT

This Master Clinical Research Services Agreement ("Agreement") is entered into as of the date of the last signature below ("Effective Date") by and between (b)(4) (b)(4) and Thermaquil, Inc. ("Company"), a Delaware Corporation. (b)(4) and Company may hereinafter be referred to collectively as the "Parties" or individually as a "Party."

WHEREAS, (b)(4) is a (b)(4) organization engaged in the business of providing (b)(4) (b)(4) and

WHEREAS, Company wishes to engage (b)(4) from time to time to provide various (b)(4) (b)(4) Company may conduct, as more fully set forth in various statements of work to be attached to this Agreement; and

Fig.1. Draft contract with the CRO (b)(4)

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Task 2.2 Clinical Study IRB Approval

(b)(4)

(b)(4)

(b)(4)

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(b)(4)

(b)(4)

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(b)(4)

(b)(4)

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(b)(4)

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1852

(b)(4)

(b)(4)

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Biocompatibility Degradation Testing Summary

(b)(4)

Work Plan for Next 4 Weeks (b)(4)

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  Obtaining IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) electrodes for human use (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

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Monthly Financial Overview

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1856

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to Report

University of Pittsburgh BG+ Monthly Status Report (b)(4)

(b)(4); (b)(6)

Reporting Period: [8/1/2022] – [8/31/2022]

8/31/2022

Overview – Technical Update

- We submitted the IRB application to the external IRB (WCG IRB) and answered the administrative questions from the external IRB. We also obtained the University's authorization to cede the IRB review to WCG IRB. (b)(4) (b)(4)
- The fourth paper for restoring female sexual function is now in proof for publication on Journal of Sexual Medicine (The proof is attached).
- (b)(4) made (b)(4) prototypes were tested at UPitt, which successfully blocked EUS and induced bladder contraction at the same time in animal study.
- All (b)(4) components have been located and are on order. (b)(4) (b)(4) All electrical and mechanical components for (b)(4) (b)(4)
-
-

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1860

Overview – Technical Update

- The biological evaluation has been defined, reviewed and approved by all parties
  - (b)(4)
- Many of the surgical kit items (b)(4)
- (b)(4)
- Continued drafting early feasibility protocol for (b)(4)
(b)(4)

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Overview – Financial Update

- University of Pittsburgh has been distributing funds monthly to (b)(4) and Thermaquil.

Overview – Administrative Update

- Administrative/progress meetings and design meetings are hold weekly to coordinate the activity among University of Pittsburgh, (b)(4) and Thermaquil.

4 Week Work Plan from Previous Report

- Task 2.2: IRB approval and NIWC HRPO approval for human studies (b)(4)
  IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) for human use (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.4: (b)(4)
  Update (b)(4) design with design review complete (b)(4)
- Task 2.5: Physician Controller ((b)(4))
  First units are tested and documentation updated to support the FDA IDE submission- (b)(4) planned (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

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COVID related updates

- Current MSR period – (b)(4) (8/1/2022-8/31/2022)
  - (b)(4)

Big Wins – The 4th paper is now in proof

ARTICLE IN PRESS

THE JOURNAL OF
SEXUAL MEDICINE

ORIGINAL RESEARCH & REVIEWS

BASIC SCIENCE

Vaginal Lubrication and Pressure Increase Induced by Pudendal Nerve Stimulation in Cats

Jialiang Chen, PhD,[1,2] Yihua Zhong, MS,[1,3] Jicheng Wang, PhD,[1] Bing Shen, DVM,[1] Zhijun Shen, PhD,[1] Jonathan Beckel, PhD,[4] William-C. de-Groat, PhD,[4] Christopher Chermansky, MD,[1] and Changfeng Tai, PhD[1,4,5]

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1866

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 8/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
2.2 IRB approval and NIWC HRPO approval for human studies (b)(4)							(b)(4)
2.2.1 Prepare and submit IRB protocols for human studies	(b)(4)					Milestone 2.2.1 – Deliverable 2.2.1	
2.2.2 Protocol review completed by NIWC HRPO						Milestone 2.2.2 – Deliverable 2.2.2	
1.4 (b)(4)							
1.4.5 Full integration and test completed for initial prototype (b)(4)	(b)(4)					Milestone 1.4.5 – Deliverable 1.4	
1.7 (b)(4) **for human use** (b)(4)							
1.7.4 Finalize design and (b)(4) production (b)(4)	(b)(4)					Milestone 1.7.4 – Deliverable 1.7	
1.7.5 Biocompatibility test is completed. Documentations for FDA submission (MAC15)						Milestone 1.7.5 – Deliverable 1.7	
1.10 Software Development Kit (SDK) (b)(4)							
1.10.2 At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API (b)(4)	(b)(4)					Milestone 1.10.2 – Deliverable 1.10	
2.4 (b)(4)							
2.4.1 Update (b)(4) design with design review complete (b)(4)	(b)(4)					Milestone 2.5.1 – Deliverable 2.5	
2.4.2 (b)(4 samples developed and fully evaluated (b)(4) (b)(4) (b)(4)						Milestone 2.5.2 – Deliverable 2.5	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1867

Milestones and Deliverables Summary

[University of Pittsburgh] Active Task Status – Past Month (b)(4) Date: 8/31/2022

SOW Task #	Planned Start	Actual Start	Due Date	Finish	Status (%)	Associated Milestone and Deliverable	Issues
2.5 Physician Controller (b)(4)							(b)(4)
2.5.1 First units are tested and documentation updated to support the FDA IDE submission (b)(4) (b)(4)	(b)(4)					Milestone 2.6.1 – Deliverable 2.6	
2.6 Patient Controller (b)(4)							
2.6.1 Firmware updates to support the latest patient configuration (b)(4)	(b)(4)					Milestone 2.7.1 – Deliverable 2.7	
2.7 (b)(4)							
2.7.1 Complete software iteration to support the latest requirements coming from the research team (b)(4)	(b)(4)					Milestone 2.8.1 – Deliverable 2.8	
2.10 (b)(4)							
2.10 (b)(4)	(b)(4)					Milestone 2.10 – Deliverable 2.10.1	
2.11 Early feasibility human clinical protocol (b)(4)							
2.11 Early feasibility human clinical protocol for (b)(4)	(b)(4)					Milestone 2.11 – Deliverable 2.11.1	
2.12 FDA IDE (b)(4)							
2.12.1 FDA IDE (b)(4) (b)(4)	(b)(4)					Milestone 2.13 – Deliverable 2.13.1	

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1868

Technical Progress Summary

- The IRB application was submitted to the external IRB (b)(4) (b)(4)
- Fourth study of restoring female sexual function is now in proof for publication.
- UPitt successfully tested (b)(4) made (b)(4) prototypes to block EUS and induce bladder contraction in the cat study.
- All (b)(4) components have been located and are on order. (b)(4) (b)(4)
- The (b)(4) to (b)(4) enclosure (b)(4) fixtures design have been re-assembled. The (b)(4)
- The (b)(4) process has been finalized. Adjustments were made (b)(4) (b)(4)
- The biological evaluation has been defined, reviewed and approved by all parties
- (b)(4)
- Continued drafting early feasibility study protocol (b)(4)
- (b)(4)

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Task 2.2 Clinical Study IRB Approval

(b)(4); (b)(6)

Fig.1. IRB submission to the external IRB (WCG).

Task 2.2 Clinical Study IRB Approval

(b)(4), (b)(6)

Figure 2: Pitt IRB cedes IRB review to WCG IRB

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Block Pudendal Nerve by Med-Ally (b)(4) Electrode Prototype

(b)(4)

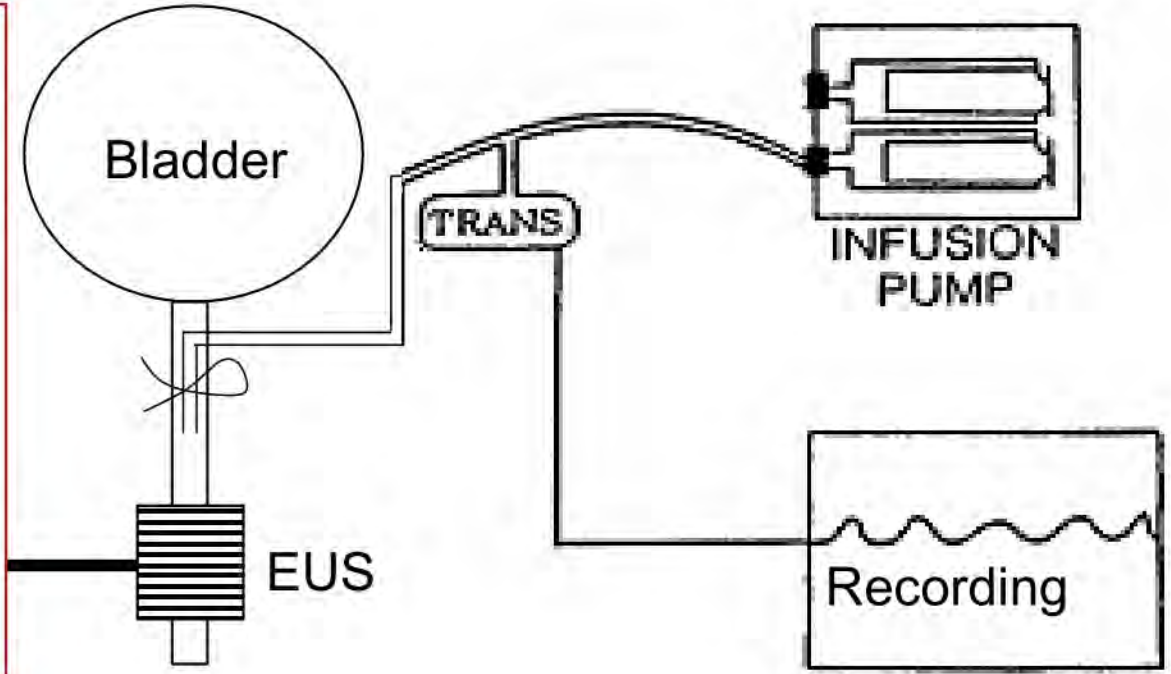

Figure 3: Experimental setup for a reversible block of pudendal nerve by (b)(4) made (b)(4) using (b)(4)
(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1872

Block Pudendal Nerve by (b)(4) Prototype

(b)(4)

WCWP v DoD, No. 23-3264 DARPA 22-F-1285 1873

Microcontroller selection

(b)(4)

Microcontroller (b)(4)

(b)(4)

Comparing MCU Choices

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

Biocompatibility Degradation Testing Summary

(b)(4)

(b)(4)

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Work Plan for Next 4 Weeks (b)(4)

- Task 2.2: IRB approval and NIWC HRPO approval for human studies using (b)(4)
  Obtaining IRB protocol approval for human studies at University of Pittsburgh (b)(4)
- Task 1.4: (b)(4)
  Full integration and test completed for initial prototype (b)(4)
- Task 1.7: (b)(4) for human use (b)(4)
  Finalize design and (b)(4) production (b)(4)
  Biocompatibility test is completed. Documentations for FDA IDE submission (b)(4)
- Task 2.4: (b)(4)
  Update (b)(4) design with design review complete (b)(4)
- Task 2.5: Physician Controller (b)(4)
  First units are tested and documentation updated to support the FDA IDE submission- (b)(4)
  (b)(4)
- Task 2.10: (b)(4)
  (b)(4)
- Task 2.11: Early feasibility human clinical protocol (b)(4)
  Preparing early feasibility human clinical protocol (b)(4)
- Task 2.12: FDA IDE (b)(4)
  Preparing FDA IDE (b)(4)

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Monthly Financial Overview

(b)(4)

Administrative issues

- Nothing to report

Miscellaneous

- Nothing to Report

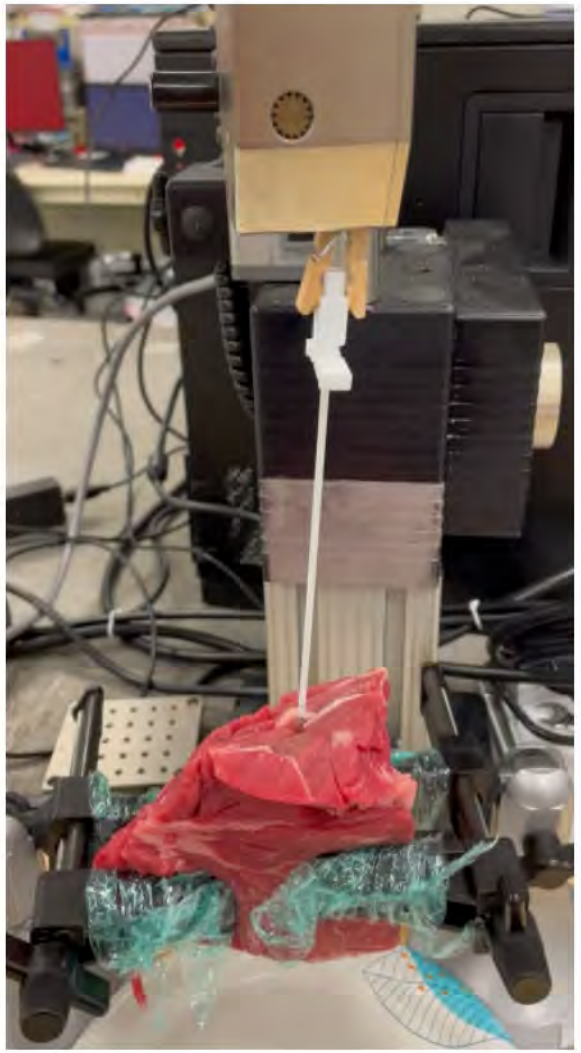
1.7.3 First prototypes of (b)(4) delivered for test

Figure 7

	Medtronic Tine Evaluation		
Max Insert Force (lbf)	Mean	Median	Standard Deviation
Introducer	(b)(4)		
Lead			
	MA Tine Evaluation		
Max Insert Force (lbf)	Mean	Median	Standard Deviation
Introducer	(b)(4)		
Lead			

- Video 1 - The Medtronic (b)(4) is inserted with a (b)(4) The current (b)(4) was inserted with a (b)(4) (b)(4) to accommodate the current (b)(4) design. The larger introducer and the tissue consistency are most likely responsible for the increased introducer insertion force.
- Video 2 - The (b)(4) inserted through the introducer at a very similar force to that of the Interstim (b)(4)
- Video 3 – The (b)(4) could not be removed from the meat due to the (b)(4) grabbing on to the surrounding tissue too well. As a result, the extrusion began to stretch. No (b)(4) were broken upon removing the (b)(4) via cutting the meat. The Interstim (b)(4) was able to be removed without the (b)(4) breaking and without stretching the extrusion.

Video 1 – Introducer/dilator insertion



Video 2 – Tined lead insertion

Video 3 – Tined lead removal

Statement of Work – ~~June~~ August 12, 2020

University of Pittsburgh
Principal Investigator: (b)(4), (b)(6)
Title: An (b)(4) System to Stabilize Acute SCI and Restore Bladder, Bowel, and Sexual Functions after Chronic SCI.

1.0 SCOPE

This effort aims to dramatically improve the functional trajectory of individuals with spinal cord injury (SCI) through restoration of bladder, bowel, and sexual function. The approach includes (b)(4) which can stimulate and record via the pudendal and (b)(4) of bladder and bowel, as well as restore sexual function. An (b)(4) and an external controller shall be developed. Initial animal testing will lay groundwork for FDA approval with the ultimate goal of human clinical trials.

This effort contains a base effort over a 60 month period of performance broken out into 3 technical (not contractual) phases.

2.0 BACKGROUND

DARPA's Bridging the Gap Plus (BG+) program seeks to develop new approaches to treating spinal cord injury by integrating injury stabilization, regenerative therapy, and functional restoration. To achieve this combinatorial approach, BG+ teams will build two systems of (b)(4) and adaptive devices. The first system (TA1) will reduce injury effects during the acute and subacute phases of spinal cord injury. This system will consist of active devices that will perform real-time biomarker monitoring and intervention to stabilize – and where possible, rebuild – the neural communications pathways at the site of injury, providing the clinician with previously unavailable diagnostic information for automated or clinician-directed interventions. The second system (TA2) will primarily address recovery of function in the chronic phase and will involve stimulation and/or recording devices that may be deployed anywhere on the nervous system or relevant end organs to effectively "bridge the gap" of the spinal cord injury.

3.0 APPLICABLE DOCUMENTS

(a) DARPA BAA- HR001120S0004
(b) UPITT Proposal Titled "An (b)(4) System to Stabilize Acute SCI and Restore Bladder, Bowel, and Sexual Functions after Chronic SCI"

4.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The Contractor shall provide the facilities and equipment necessary to develop the effort as described herein.

Human use is anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from THE GOVERNMENT (NIWC HRPO) PRIOR to human use testing.

Animal use is anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval, Secondary approval by ACURO and demonstrate this approval to the Government (NIWC) prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

Data sharing is anticipated in this effort. The recipient shall support data sharing with other performers including sharing of raw and processed experimental data, processing methods used, algorithms used to process the data, artifact information, research reports, and software including source code and executables. Data sharing shall be conducted in a manner that provides enough description for a third party to look at and conduct appropriate analysis and interpretation of the data.

1.0 Technical Phase 1 – 18 months

Animal Studies to Develop Stimulation Strategy

The purpose of these animal studies is to develop nerve stimulation/recording strategies to restore bladder, bowel, and sexual functions and test the electrode and device prototypes for nerve stimulation/recording.

1.1 Institutional IACUC approval and DOD ACURO review

1.1.1 Prepare and submit IACUC protocols for animal studies (MAC1)
Goal: To start animal studies at University of Pittsburgh
Strategy: Modify an approved protocol to achieve an early approval date
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC1) Protocols approved by University of Pittsburgh IACUC committee
Deliverable: Approved IACUC protocols

1.1.2 Prepare and submit the approved IACUC protocol for DOD review (MAC2)
Goal: To start animal studies at University of Pittsburgh
Strategy: Modify an approved protocol to achieve an early approval date
Prerequisites: IACUC approval at University of Pittsburgh
Materials & Dependencies: IACUC approval at University of Pittsburgh
Milestone: (MAC2) Protocol review completed by DOD ACURO
Deliverable: DOD ACURO approval letter

1.2 Animal studies to develop the(b)(4) system and the(b)(4) system

1.2.1 Restore bladder function (MAC3-MAC6)

Goal: To restore bladder function by(b)(4) instead of(b)(4)
Strategy: Employ our newly discovered nerve block method.
Prerequisites: None
Materials & Dependencies: This task shall use 8 anesthetized cats (2 cats for each milestone)
Milestone 1: (MAC3) Pudendal nerve block by(b)(4) is achieved in 2 cats. Pudendal nerve block is measured as urethral pressure <5 cmH2O.
Milestone 2: (MAC4) Low pressure (<50 cmH2O) voiding is induced in 2 cats.
Milestone 3: (MAC5) Number of animals is 4 for low pressure voiding to achieve statistically significant results.
Milestone 4: (MAC6) Number of animals is 6 for low pressure voiding to achieve statistical significance.
Final Deliverable: Animal experiment data/results for bladder function

1.2.2 Restore bowel function (MAC7-MAC10)

Goal: To restore bowel function in addition to the bladder function.
Strategy: The optimal result is to use the same 3 pudendal nerve(b)(4) used in task 1.2.1 to achieve the goal. If not possible, the sacral root will be stimulated by another(b)(4) or the spinal cord will be stimulated by(b)(4)
Prerequisites: None
Materials & Dependencies: This task will use 8 anesthetized cats. (2 cats for each milestone)
Milestone 1: (MAC7) Restoring defecation in 2 cats by 3 pudendal nerve(b)(4) If successful, the stimulation method shall be tested in all other cats. Defecation is measured by increase in colon pressure and elimination of the balloon catheter from the distal colon.
Milestone 2: (MAC8) Restoring defecation in 2 cats by 2 pudendal nerve(b)(4) and 1 sacral root(b)(4) If successful, the stimulation method will be tested in all other cats.
Milestone 3: (MAC9) Restoring defecation in 2 cats by 2 pudendal nerve(b)(4) in combination with magnetic stimulation of sacral spinal cord. If successful, the stimulation method will be tested in all other cats.
Milestone 4: (MAC10) Complete the last 2 cats to achieve statistical significance.
Deliverable: Animal experiment data/results for bowel function. Bowel function is restored in anesthetized SCI cats by 3(b)(4) on the pudendal nerves, or by 2(b)(4) on the pudendal nerves and 1(b)(4) on sacral root, or by 2(b)(4) on the pudendal nerves combined with spinal cord magnetic stimulation.

(b)(4)

1.2.3 Restore sexual function (MAC11-MAC14)

Goal: To restore sexual function in addition to the bladder function. For the 8 male cats, this study shall determine if pudendal nerve stimulation (PNS) alone can induce sustained (>5 minutes) and rigid penile erection. For the 8 female cats, this study will determine if PNS can induce vaginal contractions and improve vaginal lubrication.

Strategy: The optimal result is to use the same 3 pudendal nerve(b)(4) used in task 1.2.1 to achieve the goal. If not possible, the sacral root shall be stimulated by

another (b)(4) or the spinal cord shall be stimulated by (b)(4) If the nerve block can be done by (b)(4 then all other (b)(4) shall be (b)(4) If the nerve block cannot be done by (b)(4 and must use (b)(4) shall also use (b)(4 since the surgery has to expose the pudendal nerve for (b)(4 implantation anyway. In summary, there shall be no conflict for using (b)(4)

Prerequisites: None

Materials & Dependencies: This task will use 8 anesthetized male cats (2 cats for each milestone). It will also use 8 anesthetized female cats from tasks 1.2.1 and 1.2.2.

Milestone 1: (MAC11) Restoring penile erection in 2 cats by 1 pudendal nerve (b)(4 (b)(4) If successful, the stimulation method will be tested in all other cats. If not successful, the milestones 2-4 shall be performed as planned.

Milestone 2: (MAC12) Restoring penile erection in 2 cats by 1 pudendal nerve (b)(4) (b)(4) and 1 sacral root (b)(4) If successful, the stimulation method shall be tested in all other cats.

Milestone 3: (MAC13) Restoring penile erection in 2 cats by 1 pudendal nerve (b)(4) in combination with magnetic stimulation of sacral spinal cord. If successful, the stimulation method shall be tested in all other cats.

Milestone 4: (MAC14) Complete the last 2 cats to achieve statistical significance

Deliverable: Animal experiment data/results for sexual functions. Penile erection or vaginal contraction/lubrication is restored in chronic SCI cats by 1 (b)(4) on the pudendal nerve, or by 1 (b)(4) on the pudendal nerve and 1 lead electrode on sacral root, or by 1 (b)(4) on the pudendal nerve combined with spinal cord magnetic stimulation.

1.2.4 Measure fullness of bladder and bowel (MAC15-MAC17)

Goal: This task shall determine if bladder and bowel fullness can be detected by recording nerve activity from the pelvic or pudendal nerve using a (b)(4) so that the SCI subject can be notified that it is time for emptying.

Strategy: Using (b)(4) instead of (b)(4) increases the applicability to human studies.

Prerequisites: None

Materials & Dependencies: This task shall use 8 anesthetized cats (2 cats for milestone 1 and 2; 4 cats for milestone 3).

Milestone 1: (MAC15) Recording pelvic nerve activity in 2 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is if the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.

Milestone 2: (MAC16) Recording pudendal nerve activity in 2 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.

Milestone 3: (MAC17) Recording both pudendal and pelvic nerve activity in 4 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation

between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is for the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.

Deliverable: Animal experiment data/result for detecting bladder and bowel fullness

1.2.5 Test (b)(4) and device prototypes (MAC4-MAC15)

Goal: To test the (b)(4) and device prototypes. (b)(4) and devices prototypes could be tested at any stage of their development as long as the need for animal testing emerges. For example, (b)(4) needs to be tested to know the heating effect on the skin and muscle. The (b)(4) needs to be tested for its performance. The (b)(4) selection shall also need animal testing, etc.

Strategy: Prototypes shall be tested at different development stages whenever they are available for tests. Once the design of the (b)(4) and device is finalized, they shall also be tested in the on-going animal studies in tasks 1.2.1-1.2.4. The specification of the final design shall need to be determined by all the tasks in phase 1.

Prerequisites: The prototypes have completed initial design and have reached a point where testing is required.

Materials & Dependencies: Tasks 1.3-1.7. This task shall use 8 anesthetized cats.

Milestone 1: (MAC5) First prototypes of animal (b)(4) are tested to confirm the impedance is less than (b)(4) and the size/length is appropriate for cats.

Milestone 2: (MAC4) First prototype of the test bed environment is tested to confirm that it can generate the stimulation signals as designed.

Milestone 3: (MAC 11) First version (b)(4) is tested to confirm its functionality.

Milestone 4: (MAC12) First prototypes of human (b)(4) are tested to confirm the impedance is less than (b)(4)

Milestone 5: (MAC10) Wireless charging is tested to confirm its function.

Milestone 6: (MAC9) Wireless communication antenna is tested for selection.

Milestone 7: (MAC15) The (b)(4) and device prototype designs are finalized.

Deliverable: Animal experiment data/results from the tests of the (b)(4) and device prototypes

Engineering Development of the External and (b)(4)

Development of the External Stimulation System

Before (b)(4) of a (b)(4) and (b)(4) a (b)(4) device shall be used for a week to confirm efficacy and tolerability before permanent implant. The (b)(4) shall be developed to obtain FDA IDE approval at the end of Phase 1, which will allow an early feasibility study of the (b)(4) to be performed in 3 SCI human subjects in Phase 2 before testing the (b)(4) in 3 SCI subjects in Phase 3.

(b)(4)

Development of the (b)(4) System

During phase 1 the design of the (b)(4) system shall be finalized based on the animal studies, so that a fully (b)(4) system can be built and tested in phase 2 in awake animals for efficacy and safety. FDA IDE application shall be submitted at the end of phase 2. Early feasibility study shall be conducted in 3 human SCI subjects in phase 3 using the (b)(4) system after FDA IDE approval.

Tasks for Development of Both (b)(4)

1.3 Test Bed Environment (MAC1 to MAC4)

The stimulation and recording channels of this desk-top Test Bed Environment device shall be used in animal experiments as the preliminary design for the (b)(4) and the (b)(4). This test bed shall be an external test environment for the initial animal studies. The test bed shall consist of a custom (b)(4) for completing the initial stimulation and blocking output channels and recording input channels. It shall consist of the following channels with the expected features:

- Two output blocking signals will be (b)(4) (b)(4)
- One output stimulation signal will (b)(4) (b)(4)
- One or two input signals meeting:
  - (b)(4)
  - (b)(4) will be needed if recording from pudendal or pelvic nerve will work. Otherwise, (b)(4) shall be needed to record from both pelvic and pudendal nerves
- The device shall include a (b)(4) to control the configurations of the (b)(4)

The hardware design shall be based on previously developed neurostimulators, however shall be driving (b)(4) Existing stimulating devices include, on the low output scale as used for Deep Brain Stimulation (DBS), a (b)(4) to treat epilepsy. Additionally, an (b)(4) that can span (b)(4) of (b)(4) used in spinal cord injury (SCI) to treat paralysis and a 'standard SCS (b)(4) that uses (b)(4) technology. Design features of these (b)(4) shall be selected to de-risk the project, accelerate the development while cost reducing it as well.

Goal: Used to provide a test bed quickly to understand the stimulation profiles and provide the research team tools they need to get started early
Strategy: Understand the requirements, determine the components needed and build the unit as quickly as possible to act as an ongoing test bed
Prerequisites: None
Materials & Dependencies: None
Milestone 1: (MAC2) Complete initial (b)(4) schematic design with design review
Milestone 2: (MAC3) Complete initial (b)(4) fabrication/assembly and evaluation
Milestone 3: (MAC4) PC test application with (b)(4) connectivity (potentially wired or BLE depending on final requirements)

Milestone 4: (MAC4) Integration of (b)(4) in enclosure with firmware and PC application connectivity
Final Deliverable: A prototype unit for early animal research. Two set of the prototypes will be provided at MAC4 for the tasks 1.2.

1.4 (b)(4) with custom (b)(4) for animal study (Version 0) (MAC2 to MAC12)

From the development of the external test bed stimulator, the technology shall move into an (b)(4) A PC based application shall be used as initial controller. This shall be a (b)(4) (b)(4) device consisting of (b)(4) and (b)(4) with the (b)(4) The specifications for the output signals are:

1. Nerve blocking signal: (b)(4) (b)(4) **Note:** This channel/signal needs to be isolated so that it does not have cross talk to other channels/signals. The intensity can be constant or increasing gradually over minutes or hours at a step of (b)(4) (b)((b)(4 depending the output range setting. Frequency can be changed with a step of
2. Nerve blocking signal: (b)(4) (b)(4) **Note:** This channel/signal needs to be isolated so that it does not have cross talk to other channels/signals. The intensity can be constant or increasing gradually over minutes or hours at a (b)(4) (b)(4) depending the output range setting. Frequency can be changed with a step of
3. Nerve stimulation signal: (b)(4) (b)(4)
4. Nerve stimulation signal: (b)(4) (b)(4) **Note:** The need for this channel/signal shall be finalized at the phase 1 DARPA critical design review meeting.
5. Nerve stimulation signal: (b)(4) (b)(4) **Note:** The need for this channel/signal shall be finalized at the phase 1 DARPA critical design review meeting.
6. Recording channels: (b)(4) sampling rate (b)(4) **Note:** The need for these channels shall be finalized at the phase 1 DARPA critical design review meeting.

The hardware will be developed based on reference designs for similar stimulation devices. This device shall be driving (b)(4)

Goal: Build the first (b)(4) device with features focused on use in an animal study.
Strategy: Keep the focus on what is needed immediately for this initial animal study of the primary job of delivering energy to the pudendal nerve and spinal root as dictated by the researchers solely focused on the basic elements.
Prerequisites: (b)(4) Task 1.3

(b)(4)

Materials & Dependencies: None
Milestone 1: (MAC6) (b)(4) design with design review complete
Milestone 2: (MAC9) (b)(4) developed and fully evaluated (b)(4) (b)(4) etc.); evaluation consists of in house testing for a (b)(4) (b)(4) completing an electrical test on the (b)(4) and completing a pull test of the (b)(4) The acceptable leak rate for an with an (b)(4) (b)(4) This is based upon sealing in a (b)(4) environment. Test methods and (b)(4) are based upon (b)(4)

(b)(4)

Milestone 3: (MAC10) Integrate pulse generator circuit integrated into (b)(4
Milestone 4: (MAC9) Final PC test application with wireless board connectivity
Milestone 5: (MAC11) Full integration and test completed for initial prototype
Final Deliverable: Provide 5 sets of version (b)(4) to test in anesthetized normal/SCI cats in phase 1. The version is the first prototype of the (b)(4) which has included all (b)(4) as determined by the task 1.2 to restore bladder, bowel, and sexual functions.

1.5 (b)(4) for animal studies (MAC1 to MAC12)
(b)(4) specifically used on cats to assist in the research studies. These (b)(4) shall have (b)(4) at the (b)(4) The (b)(4) for stimulation or recording. The specific (b)(4) size and length shall be determined at the start of the project. Both (b)(4) are needed for animal studies. (b)(4) for stimulation and (b)(4 for recording or stimulation.

Prerequisites: None
Materials and Dependencies: None
Milestone 1: (MAC2) Finalize on the (b)(4) and length
Milestone 2: (MAC3) Finalize design of cat (b)(4)
Milestone 3: (MAC5) First prototypes of (b)(4) delivered for test
Milestone 4: (MAC7) Finalize design and (b)(4) electrode production
Final Deliverable: Provide (b)(4) for each (b)(4) developed.

1.6 (b)(4) for human study (MAC4 to MAC15)
A device that is an evolution of the (b)(4) (task 1.3) and (b)(4) (b)(4) (task 1.4) that takes the core components and embeds into a new housing with (b)(4) and uses a (b)(4) that will run for the lifetime of the 1-week study per patient. The (b)(4) is expected to be a (b)(4) and only use a (b)(4) (b)(4) if final requirements warrant.

The hardware shall be based on reference designs for similar stimulation devices. This device shall be driving more (b)(4) for the (b)(4)

Goal: Develop the initial (b)(4) into a more refined (b)(4) (b)(4) that will be used for a human study
Strategy: Build off the (b)(4) test bed, develop it to be safe and meet the FDA guidelines for an investigational device exemption
Prerequisites: (b)(4) task 1.3 and task 1.4
Materials & Dependencies: None

Milestone 1: (MAC8) Industrial design and CAD drawings for the custom enclosure
Milestone 2: (MAC10) Integration of the(b)(4) components with firmware and the enclosure
Milestone 3: (MAC15) System verification completed
Milestone 4: (MAC15) Documentation supporting the IDE submission
Milestone 5: (MAC14) Build 8 sets of(b)(4) system to conduct GLP safety study in 4 pigs in Phase 1.
Final Deliverable 1: Documentation and device are ready for IDE submission
Final Deliverable 2: Provide 8 sets of(b)(4) system to conduct GLP safety study in 4 pigs in Phase 1. Four sets will be tested, and 4 sets will be used as backup in case that replacements are needed.

1.7 (b)(4) for human use (MAC4 to MAC15)
(b)(4) to be used for human trials and would start with the(b)(4) device for the investigational device exemption submission. The(b)(4) shall support stimulation and recording of signals. The stimulation(b)(4 may be used to support(b)(4)
The recording shall support(b)(4) for the(b)(4) Both (b)(4) are needed for the final(b)(4) for initial(b)(4) be a backup plan for the surgeon and patient to decide if the(b)(4 migration becomes a problem after initial success. However, the(b)(4) will be developed(b)(4) for human(b)(4) use in phase 2 and eventually for human(b)(4 use in phase 3, but shall be developed in phase 1 for animal testing and in phase 2 for human use.

Prerequisites: None
Materials and Dependencies: None
Milestone 1: (MAC4) Finalize on the size and length
Milestone 2: (MAC8) Finalize design of human
Milestone 3: (MAC12) First prototypes of delivered for test
Milestone 4: (MAC15) Finalize design and production
Milestone 5: (MAC15) Biocompatibility test is completed. Documentations for FDA IDE submission
Final Deliverable: Provide three to five(b)(4) for each(b)(4) developed. Provide documentations for FDA IDE submission.

1.8 Physician/Investigator controller for human(b)(4) and animal(b)(4 (MAC6 to MAC10)
Develop a(b)(4) that can configure the(b)(4) as detailed in the requirements. The physician/investigator(b)(4) shall have a wider ability to control the (b)(4) The initial features shall be:

- (b)(4) or (b)(4) as needed.
- Program the(b)(4) to a certain set of(b)(4) that is determined by the physician to be effective.
- One physician(b)(4) shall be able to control many(b)(4)

Goal: Provide a standalone(b)(4) for configuration and control of the(b)(4) The (b)(4) is expected to be a(b)(4) to connect to

either the (b)(4) The (b)(4) shall use a (b)(4) that can be customized for use as a Physician (b)(4) and easily updated to be used as the Patient (b)(4)
Strategy: Focus is on functionality and less on the industrial design of the device. Make it user friendly and work to meet the research needs
Prerequisites: Build in parallel with (b)(4) Tasks 1.4 and 1.5
Materials & Dependencies: None
Milestone 1: (MAC9) Schematic design complete
Milestone 2: (MAC11) Evaluation board fabricated/assembled and initial evaluation complete
Milestone 3: (MAC12) Integration with a simple enclosure with display and firmware
Milestone 4: (MAC15) Final documentation to support the FDA IDE as an accessory device
Final Deliverable: Investigator controller meets the requirements to control the (b)(4) to support the animal studies and for human study with FDA IDE for (b)(4)

1.9 Patient (b)(4) for human (b)(4) (MAC8 to MAC11)
Develop a (b)(4) that can trigger the (b)(4) as programmed during the initial (b)(4) placement. The (b)(4) shall have a limited ability to control the (b)(4) (b)(4) It will be built exactly as a (b)(4) with limited capabilities. Meaning the (b)(4) is a software change only compared to the (b)(4) The initial features will be:

- Simple (b)(4) to trigger the (b)(4) to perform the function as programed by the physician.
- A (b)(4) will be supplied with every (b)(4)

Goal: Used when a patient is home with the (b)(4)
Strategy: Develop a simpler (b)(4) with very selective configurations/control
Prerequisites: (b)(4) Task 1.6
Materials & Dependencies: None
Milestone 1: (MAC12) Firmware features complete to restrict use as a (b)(4)
Milestone 2: (MAC13) Verification testing completed
Final Deliverable: (b)(4) meets the requirements to control the (b)(4) for human use to support the IDE study for Phase 2.

1.10 Software Development Kit (SDK) (MAC4 to MAC15)
The SDK will be developed as part of the firmware development for the (b)(4) The requirements for the SDK will be established at the start of the initial development so it is understood what may be exposed to future researchers. The SDK will then provide an exposure via an application programmer's interface (API) for what custom software can be developed to access the functions of either the (b)(4)

Goal: Allow for future researchers use the platform for their own research and development.
Strategy: Develop an understanding of the requirements DARPA wants to provide and develop the software and documentation detailing the API
Prerequisites: None
Materials & Dependencies: Functioning (b)(4)
Milestone 1: (MAC6) Requirements understood for SDK

Milestone 2: (MAC15) At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API
Final Deliverable: Source Code, Library and documentation for the SDK

GLP Safety Study, Human Cadaver Study, and FDA Regulatory Submission

Development of the External Stimulation System

1.11 GLP animal study (MAC14-MAC15)
Goal: To collect safety data to support the FDA IDE submission.
Strategy: The external system shall be tested in 4 awake normal pigs for 1 week.
Prerequisites: Eight sets of the external system.
Materials & Dependencies: Engineering progress from Tasks 1.5-1.7
Milestone: (MAC15) GLP safety study is completed for the external system
Deliverable: GLP safety study data for the external system and related documentation for FDA IDE submission

1.12 Human cadaver study (MAC2-MAC10)
Goal: To develop surgical approach and tools for the external system
Strategy: Using cadaver to determine the length of the(b)(4) and the location of the(b)(4) A surgical plan shall also be developed.
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC10) Cadaver study is completed with a total of 3 cadavers.
Deliverable: Documentation for surgical approach and the design documentation of the insertion tools for the external system

1.13 Early feasibility human clinical protocol for(b)(4) system (MAC2-MAC15)
This protocol will be submitted to FDA in the first pre-submission meeting.
Goal: To write and align on the human early feasibility study protocol to be executed in Phase 2.
Strategy: We will use our previous protocol developed for the PSTIM technology as the reference to form this new protocol.
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC15) Human clinical protocol is ready for inclusion in pre-submission to FDA.
Deliverable: Complete early feasibility clinical study protocol.

1.14 FDA IDE pre-submission #1 (MAC3-MAC5)
1.14.1 FDA IDE pre-submission #1 for the external stimulation system
Goal: To get early feedback from FDA about the device testing plan
Strategy: In this submission we will review our plans for pre-clinical and cadaver testing of the(b)(4) system.
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC3) FDA IDE pre-submission #1 is sent to FDA for the external stimulation system
Deliverable: FDA IDE pre-submission #1 documentation for the external stimulation system and all related FDA communications

1.14.2 FDA IDE pre-submission #1 meeting
Goal: To get early feedback from FDA about our device testing plan
Strategy: In this meeting we will review our plans for pre-clinical and cadaver testing of the(b)(4) system.
Prerequisites: Pre-submission #1
Materials & Dependencies: FDA review process
Milestone: (MAC5) FDA IDE pre-submission #1 meeting is completed for the external stimulation system.
Deliverable: FDA IDE pre-submission #1 meeting documentation for the external stimulation system and all related FDA communication

1.15 FDA IDE pre-submission #2 (MAC8-MAC10)
1.15.1 FDA IDE pre-submission #2 for the external stimulation system
Goal: To get feedback from FDA about our device
Strategy: In this submission we shall review our plans for clinical testing of the(b)(4) system and ask any final questions in preparation for IDE submission.
Prerequisites: Pre-submission #1 meeting
Materials & Dependencies: FDA review process
Milestone: (MAC8) FDA IDE pre-submission #2 is completed for the external stimulation system
Deliverable: FDA IDE pre-submission #2 documentation for the external stimulation system and all related FDA communication
1.15.2 FDA IDE pre-submission #2 meeting
Goal: To get feedback from FDA about our device
Strategy: In this meeting we will review our plans for clinical testing of the(b)(4) system and ask any final questions in preparation for IDE submission.
Prerequisites: Pre-submission #2
Materials & Dependencies: FDA review process
Milestone: (MAC10) FDA IDE pre-submission #2 meeting is completed for the external stimulation system
Deliverable: FDA IDE pre-submission #2 meeting documentation for the external stimulation system and all related FDA communication

1.16 FDA IDE submission (MAC15-MAC18)
1.16.1 Prepare and submit FDA IDE application for the external stimulation system
Goal: To obtain FDA IDE approval
Strategy: In this submission the contractor shall include all documents required by FDA in previous pre-submission meetings.
Prerequisites: Pre-submission #2 meeting
Materials & Dependencies: Tasks 1.5-1.7, Tasks 1.8-1.10
Milestone: (MAC15) FDA IDE application for the external stimulation system is submitted
Deliverable: FDA IDE submission for the external stimulation system and all related FDA communication
1.16.2 FDA IDE approval for the external stimulation system
Goal: To obtain FDA IDE approval

Strategy: In this submission the contractor shall include all documents required by FDA in previous pre-submission meetings.
Prerequisites: FDA IDE submission
Materials & Dependencies: FDA review process
Milestone: (MAC18) IDE approved by FDA for the external stimulation system
Deliverable: FDA IDE approval for the external stimulation system and all related FDA communication

DARPA Review

1.17 DARPA preliminary design review (MAC12)
Goal: To obtain DARPA approval for project continuation
Strategy: Prepare documentations for preliminary design review
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC12) DARPA preliminary design review is completed
Deliverable: Preliminary design documentation

1.18 DARPA critical design review (MAC15)
Goal: To obtain DARPA approval for project continuation
Strategy: Prepare documentations for critical design review
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC15) DARPA critical design review is completed
Deliverable: Phase 1 system design documentation

1.19 Final demonstration and report (MAC18)
Goal: To obtain DARPA approval to continue this contract into phase 2
Strategy: Prepare documentations for final demonstration
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC18) Phase 1 final demonstration and report are completed
Deliverable: Phase 1 final report

2.0 Technical Phase 2 – 24 months

Non-GLP Animal Study and Human Study for Efficacy

The contractor shall conduct non-GLP animal studies to determine the efficacy of the (b)(4) system to support the FDA IDE submission. The contractor shall also conduct a clinical trial to determine the feasibility and possible benefit of the external stimulation system in SCI human subjects.

2.1 Non-GLP animal study using the (b)(4) system

The purpose of this Non-GLP study is to obtain pre-clinical efficacy data to support the FDA IDE submission for the implantable system.

2.1.1 Non-GLP animal study in normal cats (MAC21-MAC27)

Goal: To confirm the functionality of the (b)(4) before testing in awake chronic SCI cats. The metric of success includes: 1. The (b)(4) system functions as designed, i.e. it can provide the required (b)(4) function; 2. The physiology functions can be restored including bladder, bowel, and sexual functions.

Strategy: Conduct this study in 4 groups of cats (2 cats per group) so that improvements to the system can be made after each testing group.

Prerequisites: Eight sets of the (b)(4) system for testing.

Materials & Dependencies: Task 2.4. The contractor shall provide 8 sets of version #1 (b)(4) for Pitt to test. This task will use 8 anesthetized normal cats (2 cats for each milestone so that change/improvement can be included in the next milestone). The change/improvements may be needed for: software bugs, (b)(4) connector/cable issues, and potential minor modification of the electronics, or (b)(4) modification, etc.

Milestone 1: (MAC21-MAC22) Version #1 (b)(4) is tested in 2 cats

Milestone 2: (MAC23-MAC24) Improved version #1 (b)(4) is tested in 2 cats

Milestone 3: (MAC25-MAC26) Improved version #1 (b)(4) is tested in 2 cats

Milestone 4: (MAC26-MAC27) Improved version #1 (b)(4) is tested in 2 cats

Deliverable: Animal experiment data/results for the version of the (b)(4) (b)(4)

2.1.2 Non-GLP animal study in awake SCI cats (MAC27-MAC39)

Goal: To determine the efficacy of the (b)(4) system in awake chronic SCI cats to support the FDA IDE submission. The metric of success includes: 1. The (b)(4) system functions as designed, i.e. it can provide the required stimulation/blocking/recording function; 2. The physiology functions can be restored including bladder, bowel, and sexual functions.

Strategy: Conduct this study in 4 group of cats (2 cats per group) so that improvements to the system can be made after each testing group.

Prerequisites: 16 sets of the (b)(4) system for testing.

Materials & Dependencies: Task 2.1.1. This task shall use 8 awake chronic SCI cats (2 cats for each milestone so that change/improvement can be included in the next milestone). The change/improvements may be needed for: software bugs, (b)(4) connector/cable issues, and potential minor modification of the electronics, or

(b)(4)

(b)(4) modification, etc.(b)(4) will provide 16 sets of the (b)(4) for testing.
Milestone 1: (MAC27-MAC31) Version (b)(4) is tested in 2 cats
Milestone 2: (MAC30-MAC34) Improved version (b)(4) is tested in 2 cats
Milestone 3: (MAC33-MAC37) Improved version is tested in 2 cats
Milestone 4: (MAC35-MAC39) Improved version is tested in 2 cats
Deliverable: Animal experiment data/results for the version of the (b)(4) system

(b)(4)

2.2 IRB approval and NIWC HRPO approval for human studies using the external stimulation system

2.2.1 Prepare and submit IRB protocols for human studies (MAC19)
Goal: To start human studies at University of Pittsburgh
Strategy: Prepare the IRB submission before FDA IDE approval to save time
Prerequisites: FDA IDE approval of the external stimulation system
Materials & Dependencies: FDA IDE approval of the external stimulation system
Milestone: (MAC19) Protocols approved by University of Pittsburgh IRB committee
Deliverable: Approved IRB protocols

2.2.2 Prepare and submit the approved IRB protocol for NIWC review (MAC20)
Goal: To start human studies at University of Pittsburgh
Strategy: Prepare for NIWC review before IRB approval to save time
Prerequisites: IRB approval at University of Pittsburgh
Materials & Dependencies: IRB approval at University of Pittsburgh
Milestone: (MAC20) Protocol review completed by NIWC HRPO
Deliverable: NIWC HRPO approval letter

2.3 Early feasibility study in human SCI subjects using the external stimulation system

2.3.1 Human SCI study preparation and subject recruitment (MAC20-MAC30)
A total of 3 SCI human subjects will be recruited.
Goal: To determine the feasibility and possible benefit of the external stimulation system.
Strategy: Non-sequential enrollment will be employed to start the study.
Prerequisites: FDA IDE approval, IRB approval, and NIWC HRPO approval
Materials & Dependencies: Task 2.8: Contractor shall provide 9 sets of the FDA IDE approved external stimulation system for testing.
Milestone: (MAC30) First human subject is enrolled
Deliverable: First human subject enrollment documentation

2.3.2 Conduct human clinical study (MAC30-MAC42)
Goal: To determine the feasibility and possible benefit of the external stimulation system.(b)(4) will be placed close to the pudendal nerves in 3 SCI human subjects by (b)(4) to restore bladder, bowel, and sexual function. The(b)(4) shall be connected to the(b)(4) for the subjects to test them during a 1-week period. The success is evaluated by: 1. Low-pressure (<50 cmH2O) voiding is induced with >50% efficiency; 2. Defecation is induced so that constipation can be avoided; 3. Penile erection for male and vaginal contraction/wetness for female are achieved as needed. The contractor shall meet the

DARPA BAA metrics: 1. Clinical transition ≥ 1 clinical sponsor; 2. # of functions addressed in humans ≥ 2; 3. Functional improvement in humans 3x over baseline (The baseline for these functions in complete SCI subject is none, so we are certain that we will achieve this goal).
Strategy: Testing one subject at a time to ensure the completion of the study
Prerequisites: FDA IDE approval, IRB approval, and NIWC HRPO approval
Materials & Dependencies: Task 2.8: Contractor shall provide 9 sets of the FDA IDE approved external stimulation system for testing. The 3 sets of system will be used by the 3 human subjects and 6 sets of the system will be used as backup in case that anything is broken during 1-week testing period,
Milestone 1: (MAC34) First SCI subject test is completed
Milestone 2: (MAC38) Second SCI subject test is completed
Milestone 3: (MAC42) Human clinical study is completed with 3 SCI subjects tested
Deliverable: Data and documentation of early feasibility study of the external stimulation system

Tasks 2.3.1 and 2.3.2 contain Human Subject Research (HSR). Work shall not proceed until IRB protocols have been approved, and NIWC HRPO approval letter has been received by contractor.

Engineering Development of the(b)(4)

Tasks for Development of(b)(4) for Human Use and Supporting Systems

2.4 (b)(4) with Custom (b)(4) for Animal Study (Version 1/2) (MAC21-MAC27)
In supporting the continuing animal studies, the contractor shall complete a final version of the(b)(4) for the animal study with all the(b)(4) and requested configurations from research. An evolution may also be required via software changes to meet the new requirements to support the second animal study completed in this phase.

(b)(4)

Goal: Continue supporting the animal study research
Prerequisites:(b)(4) from Phase 1 and the final(b)(4) design based on the animal studies from Phase 1
Materials & Dependencies: None
Milestone 1: (MAC21-MAC27) Update to Version 1 to meet any new requirements and/or fix issues found during animal testing in Phase 1
Milestone 2: (MAC19-MAC27) Build 8 sets of the version 1 and improved version 2 (b)(4) system for testing in 8 anesthetized cats
Deliverable: Provide 8 sets of the version 1 and/or improved version 2(b)(4) system for testing in 8 anesthetized cats
Milestone 3: (MAC27) Update to Version 2 to meet any new requirements and/or fix issues found during the continuing animal studies in Phase 2.
Final Deliverable: Version 2 for testing in awake chronic SCI cats

(b)(4)

(b)(4)

(b)(4)

(b)(4)

2.5 (b)(4) (Support Animal Trials and IDE Human Use) (MAC23-MAC31)
This would be the start of the (b)(4) for human use development focused on the evolution of the work completed during Phase 1.
The work shall include updating the (b)(4) for the needs for human testing and potential change in the type of battery used to meet the longevity goals of the (b)(4) The number of (b)(4) required may change depending on the perceived need coming from the early animal trials and/or potentially studies started with the (b)(4) (b)(4) device. Human (b)(4) development shall also be completed with this human (b)(4)

(b)(4)
(b)(4)

Goal: Develop an (b)(4) that will receive FDA IDE approval for use in humans in a clinical trial that is MRI compatible.
Prerequisites: (b)(4) from Phase - and the final (b)(4) design based on the animal studies from Phase -
Materials & Dependencies: None
Milestone 1: (MAC23) Update (b)(4) Design with Design Review Complete
Milestone 2: (MAC25) (b)(4) samples developed and fully evaluated (b)(4) (b)(4)
Milestone 3: (MAC27) (b)(4) circuit integrated into (b)(4)
Milestone 4: (MAC28) Complete longevity study; the contractor shall use prediction tools to evaluate the reliability of the electronics at the expected stress levels. (b)(4) longevity will be supplied by the chosen (b)(4) manufacturer. Completion of accelerated life testing.
Deliverable: Build 16 sets of the version (b)(4) system for testing in 8 awake SCI cats.
Milestone 5: (MAC31) Full Integration and test completed for initial prototype
Milestone 6: (MAC31) Biocompatibility test is completed.
Milestone 7: (MAC31) Human (b)(4) development is completed and documentations are ready for FDA IDE submission.
Final Deliverable: Build 16 sets of the final version (b)(4) system to conduct safety GLP studies of 8 awake pigs. Provide documentations for FDA IDE submission.

(b)(4)

2.6 Physician (b)(4) (MAC21-MAC29)
The contractor shall update the (b)(4) developed during Phase - It shall be developed closer to the final product and go through conceptual and industrial design and usability via discussions with clinicians. For the electronics, the plan shall be to continue to use an (b)(4) (b)(4) with the proper (b)(4) communication modules for the communication technology chosen (b)(4) The contractor shall then focus on providing firmware updates as needed to meet final requirements for the (b)(4)
An initial upgrade to complete the final enclosure and integrate the (b)(4) into the unit is planned. A second iteration is planned for future upgrades that may be requested as research is ongoing.

Milestone 1: (MAC21) First units are tested and documentation updated to support the FDA IDE submission; three units are planned

Milestone 2: (MAC29) Units are upgraded for new requirements to support additional configurations (software only)
Final Deliverable: Provide 3 (b)(4) with supporting documentation to support an FDA IDE submission and the ongoing animal trials and for the human clinical in Phase 3

2.7 (b)(4) (MAC23-MAC30)
The contractor shall update the (b)(4) developed during Phase - It shall be developed closer to the final product and go through conceptual and industrial design and usability via discussions with clinicians. The firmware shall be updated per requests from the research team. Two potential iterations are planned. The (b)(4) shall be based on the (b)(4) with limited controls. The first iteration shall occur after the first iteration of the (b)(4) are completed.

Milestone 1: (MAC23) Firmware updates to support the latest patient configurations
Milestone 2: (MAC30) Second iteration of firmware updates to support the latest patient configurations
Final Deliverable: Build 9 units to support each of the human (b)(4) devices for Phase 3

Tasks for Development of (b)(4) for Human Use and Supporting Systems

2.8 (b)(4) for Human Study (MAC25)
Focus shall be supporting the clinical work occurring using the FDA IDE. The updates would be focused on software updates to make configuration changes requested and fix any potential issues. There are plans for one software iteration.

Goal: Continue supporting the clinical study research
Prerequisites: Research Requests (b)(4) from Phase -
Materials & Dependencies: None
Milestone: (MAC25) Complete software iteration to support the latest requirements coming from the research team.
Final Deliverable: Build 9 sets of the FDA IDE approved external stimulation system for testing in human studies

Safety Study, FDA Regulatory Submission, and Clinical Trial Management

Development of the (b)(4) System

2.9 GLP animal study (MAC31-MAC39)
Goal: To collect safety data to support the FDA IDE submission.
Strategy: The (b)(4) system will be tested in 8 awake normal pigs for 12 weeks by a CRO – CBSET Inc.
Prerequisites: Delivery of (b)(4) for testing.
Materials & Dependencies: (b)(4)
Milestone: (MAC39) GLP safety study is completed for the (b)(4)
Deliverable: GLP safety study data for the (b)(4) and related documentation for FDA IDE submission

2.10 Human cadaver study (MAC21-MAC23) The contractor shall develop a surgical approach and tools for the implantable system.
Goal: To develop surgical approach and tools for the (b)(4) system
Strategy: Using cadaver to determine the length of the (b)(4) and the location of the (b)(4) A surgical plan shall also be developed.
Prerequisites: Design freeze of the (b)(4) system
Materials & Dependencies: Design freeze of the (b)(4) system
Milestone: (MAC23) Cadaver study is completed with a total of 3 cadavers.
Deliverable: Documentation of surgical approach and design documentation of (b)(4) tools for the (b)(4)

2.11 Early feasibility human clinical protocol for (b)(4) system (MAC19-MAC26)
This protocol shall be submitted to FDA in the second pre-submission.
Goal: To write and align on the human feasibility study protocol to be executed in Phase 3.
Strategy: The contractor shall use our previous protocol developed for the (b)(4) technology as the reference to form this new protocol.
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC26) Human clinical protocol is ready for inclusion in pre-submission to FDA.
Deliverable: Complete feasibility clinical study protocol.

2.12 FDA IDE pre-submissions #1 for the (b)(4)

2.12.1 FDA IDE pre-submission #1 for the (b)(4) (MAC20)
Goal: To get early feedback from FDA about (b)(4)
Strategy: In this submission the contractor shall review our plans for pre-clinical and cadaver testing of the (b)(4) system. As compared to Informational meetings, which are primarily to inform FDA about new projects while receiving only general guidance, this submission shall address specific questions and solicit direct feedback from the FDA.
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC20) FDA IDE pre-submission #1 is completed for the (b)(4) system
Deliverable: FDA IDE pre-submission #1 documentation for the (b)(4) and all related FDA communication

2.12.2 FDA IDE pre-submission #1 meeting (MAC22)
Goal: To get early feedback from FDA about plans for pre-clinical and cadaver device testing.
Strategy: In this submission the contractor shall review our plans for pre-clinical and cadaver testing of the (b)(4) As compared to Informational meetings, which are primarily to inform FDA about new projects while receiving only general guidance, this submission shall address specific questions and solicit direct feedback from the FDA.
Prerequisites: Pre-submission #1

Materials & Dependencies: FDA review process
Milestone: (MAC22) FDA IDE pre-submission #1 meeting is completed for the (b)(4) system
Deliverable: FDA IDE pre-submission #1 meeting documentation for the implantable system and all related FDA communication

2.13 FDA IDE pre-submissions #2 for the (b)(4) system

2.13.1 FDA IDE pre-submission #2 for the implantable system (MAC26)
Goal: To get feedback from FDA about our benchtop device safety testing plans
Strategy: In this submission the contractor shall review our plans for safety testing of the (b)(4) system.
Prerequisites: Pre-submission #1 meeting
Materials & Dependencies: FDA review process
Milestone: (MAC26) FDA IDE pre-submission #2 is completed for the (b)(4) system
Deliverable: FDA IDE pre-submission #2 documentation for the (b)(4) system and all related FDA communication

2.13.2 FDA IDE pre-submission #2 meeting (MAC28)
Goal: To get feedback from FDA about our device
Strategy: In this meeting the contractor shall review our plans for clinical testing of the (b)(4) system and ask any questions in preparation for IDE submission.
Prerequisites: Pre-submission #2
Materials & Dependencies: FDA review process
Milestone: (MAC28) FDA IDE pre-submission #2 meeting is completed for the implantable system.
Deliverable: FDA IDE pre-submission #2 meeting documentation for the (b)(4) system and all related FDA communication

2.14 FDA IDE pre-submissions #3 for the (b)(4) system
In this meeting the contractor shall review our plans for clinical testing of the (b)(4) system and ask any final questions in preparation for IDE submission.

2.14.1 FDA IDE pre-submission #3 for the (b)(4) system (MAC35)
Goal: To get feedback from FDA about our device clinical testing plan
Strategy: In this submission the contractor shall review plans for clinical testing of the (b)(4) system and ask any questions in preparation for IDE submission.
Prerequisites: Pre-submission #2 meeting
Materials & Dependencies: clinical testing protocol
Milestone: (MAC35) FDA IDE pre-submission #3 is completed for the (b)(4) system
Deliverable: FDA IDE pre-submission #3 documentation for the (b)(4) system and all related FDA communication

(b)(4)

2.14.2 FDA IDE pre-submission #3 meeting (MAC37)
Goal; To get feedback from FDA about our device
Strategy: In this meeting the contractor shall review plans for clinical testing of the (b)(4) system and ask any questions in preparation for IDE submission.
Prerequisites: Pre-submission #3

Materials & Dependencies: FDA review process
Milestone: (MAC37) FDA IDE pre-submission #3 meeting is completed for the (b)(4) system
Deliverable: FDA IDE pre-submission #3 meeting documentation for the (b)(4) system and all related FDA communication

2.15 FDA IDE submission for (b)(4) system

2.15.1 Prepare and submit FDA IDE application for the (b)(4) system (MAC39)
Goal: To obtain FDA IDE approval
Strategy: In this submission the contractor shall include all documents required by FDA in previous pre-submission meetings.
Prerequisites: Pre-submission #3 meeting
Materials & Dependencies: FDA review process
Milestone: (MAC39) FDA IDE application for the (b)(4) system is submitted
Deliverable: FDA IDE submission for the (b)(4) system and all related FDA communication

2.15.2 FDA IDE approval for the (b)(4) system (MAC42)
Goal: To obtain FDA IDE approval
Strategy: In this submission the contractor shall include all documents required by FDA in previous pre-submission meetings.
Prerequisites: FDA IDE submission
Materials & Dependencies: FDA review process
Milestone: (MAC42) IDE approved by FDA for the (b)(4) system
Deliverable: FDA IDE approval for the (b)(4) system and all related FDA communication

Development of the (b)(4) Stimulation System

2.16 Clinical trial preparations and enrollment (MAC19-MAC42)
Goal: To ensure a successful initiation and enrollment of the clinical trial
Strategy: The contractor shall prepare for the overall success of the human trial. This shall include responsibility for preparing site training materials, site binders, processes to collect, analyze and manage data, contingency planning and ensuring access to sufficient patients to complete the clinical trial.
Prerequisites: FDA IDE approval, IRB, and NIWC HRPO approval.
Materials & Dependencies: None
Milestone: (MAC30) First subject enrolled in (b)(4) study.
Deliverable: Documentation of treatment of first subject using (b)(4) system.

2.17 Clinical trial management (MAC19-MAC42)
Goal: To ensure a successful completion of the clinical trial
Strategy: As study Sponsor, the contractor is accountable for the overall success of the human trial. This includes responsibility for site training, compliance including proper documentation, data collection processes, data analysis and management, and ensuring successful completion and write-up the clinical trial.
Prerequisites: FDA IDE approval, IRB, and NIWC HRPO approval.

Materials & Dependencies: None
Milestone: (MAC42) Three subjects treated using(b)(4) system.
Deliverable: Clinical trial report.

Tasks 2.16 and 2.17 contain Human Subject Research (HSR). Work shall not proceed until IRB protocols have been approved, and NIWC HRPO approval letter has been received by contractor.

DARPA Review

2.18 Phase 2 demonstration and report

2.18.1 Prepare phase 2 animal demonstration of the(b)(4) system
Goal: To obtain DARPA approval to continue this contract into phase 3
Strategy: Prepare documentations for phase 2 demonstration
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC42) Phase 2 animal demonstration and report are completed
Deliverable: Phase 2 final report

2.18.2 Prepare phase 2 clinical demonstration of the(b)(4) stimulation system
Goal: To obtain DARPA approval to continue this contract into phase 3. The specifications for this demonstration include: 1. The success of human(b)(4) studies, which means successfully restoring bladder, bowel, sexual functions in 3 human SCI subjects over a 1-week period; 2. The success of chronic animal studies, which means successfully restoring bladder, bowel, sexual functions in awake chronic SCI cats for 3 months; 3. FDA IDE approval of the human so that it can be tested in phase 3.
Strategy: Prepare documentations for phase 2 demonstration
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC42) Phase 2 clinical demonstration and report are completed
Deliverable: Phase 2 final report

(b)(4)
(b)(4)

3.0 Technical Phase 3 – 18 months

Human Study of the (b)(4) System

3.1 IRB approval and NWIC HRPO approval for human studies using the (b)(4) system

3.1.1 Prepare and submit IRB protocols for human studies (MAC43)
Goal: To start human studies
Strategy: Prepare the IRB submission before FDA IDE approval to save time
Prerequisites: FDA IDE approval of the (b)(4) system
Materials & Dependencies: FDA IDE approval of the implantable system
Milestone: (MAC43) Protocols approved by University of Pittsburgh IRB committee
Deliverable: Approved IRB protocols

3.1.2 Prepare and submit the approved IRB protocol for NIWC review (MAC44)
Goal: To start human studies
Strategy: Prepare for NIWC review before IRB approval to save time
Prerequisites: IRB approval
Materials & Dependencies: IRB approval
Milestone: (MAC44) Protocol review completed by NIWC HRPO
Deliverable: NIWC HRPO approval letter

3.2 Early feasibility study in human SCI subjects using the (b)(4) system

3.2.1 Human SCI subject recruitment (MAC44-MAC47)
Goal: To determine the feasibility and possible benefit of the (b)(4) system.
Strategy: Non-sequential enrollment will be employed to start the study.
Prerequisites: FDA IDE approval, IRB approval, and NIWC HRPO approval
Materials & Dependencies: 9 sets of the FDA IDE approved (b)(4) system for testing. A total of 3 SCI human subjects shall be recruited.
Milestone: (MAC47) First human subject is enrolled
Deliverable: First human subject enrollment documentation

3.2.2 Conduct human clinical study (MAC47-MAC59)
Goal: To determine the feasibility and possible benefit of the (b)(4) system. The success is evaluated by: 1. Low-pressure (<50 cmH2O) voiding is induced with >50% efficiency; 2. Defecation is induced so that constipation can be avoided; 3. Penile erection for male and vaginal contraction/wetness for female are achieved as needed. The contractor shall meet the DARPA BAA metrics: 1. Clinical transition ≥ 1 clinical sponsor; 2. # of functions addressed in humans ≥ 2; 3. Functional improvement in humans 3x over baseline (The baseline for these functions in complete SCI subject is none, so we are certain that we will achieve this goal).
Strategy: Testing one subject at a time to ensure the completion of the study
Prerequisites: FDA IDE approval, IRB approval, and NIWC HRPO approval
Materials & Dependencies: The contractor shall provide 9 sets of the FDA IDE approved (b)(4) system for testing.
Milestone 1: (MAC51) First human subject test is completed
Milestone 2: (MAC55) Second human subject text is completed
Milestone 3: (MAC59) Human clinical study is completed with 3 SCI subjects tested

Commented [BS1]: Should there be any intermediate milestones over the 12 month period, specifying timelines for each subject (b)(4) testing procedures, metrics to assess benefit etc. ?

Deliverable: Data and documentation of early feasibility study of the (b)(4) (b)(4) system

Tasks 3.2.1 and 3.2.2 contain Human Subject Research (HSR). Work shall not proceed until IRB protocols have been approved, and NIWC HRPO approval letter has been received by contractor.

Engineering and Manufacturer Support to Human Study

3.3 (b)(4) for Human Use (MAC47-MAC59)

Device updates supporting the clinical trial as feature requests are presented or bugs are found. The contractor shall make updates as they are presented and the change control board approves. The timing of when these changes shall be determined as the need requires based on previous results.

(b)(4)

(b)(4)

Goal: Continue supporting the clinical study research
Prerequisites: Research Requests, (b)(4) from Phase 1
Materials & Dependencies: None
Milestone 1: (MAC47) Build 9 sets of the FDA IDE approved system for testing in human studies
Deliverable 1: Provide 9 sets of the FDA IDE approved system for testing in human studies
Milestone 2: (MAC59) Provide device support and update devices or build new ones depending on the requested changes to support the research team. Any updates made that affect the requirements or potential risk shall be updated. For verification of updates, the engineering team with the regulatory team shall decide what type of testing is needed (full re-run of verification vs regression) and then testing shall be executed with the proper reports.
Deliverable 2: Updated devices as required.

3.4 (b)(4) (MAC47-MAC59)

Device updates supporting the clinical trial as feature requests are presented or bugs are found. The (b)(4) shall be a support device to test (b)(4) placement and effectiveness before (b)(4) The contractor shall make the updates as they are presented and the change control board approves. The timing of when these changes shall be determined as the need requires based on previous results.

Goal: Continue supporting the clinical study research
Prerequisites: Research Requests, (b)(4) from Phase 1
Materials & Dependencies:
Milestone 1: (MAC47) Build 9 sets of the FDA IDE approved (b)(4) system for testing in human studies

Deliverable 1: Provide 9 sets of the FDA IDE approved (b)(4) system for testing in human studies
Milestone 2: (MAC59) Provide device support and update devices or build new ones depending on the requested changes to support the research team. Any updates made that affect the requirements or potential risk shall be updated. For verification of updates, the engineering team with the regulatory team shall decide what type of testing is needed (full re-run of verification vs regression) and then testing shall be executed with the proper reports.
Deliverable 2: Updated devices as required.

Clinical Trial Management

3.5 Clinical trial preparations and enrollment (MAC43-MAC60)
Goal: To ensure a successful initiation and enrollment of the clinical trial
Strategy: As study Sponsor, the contractor is accountable for the overall success of the human trial. This includes responsibility for preparing site training materials, site binders, processes to collect, analyze and manage data, contingency planning and ensuring access to sufficient patients to complete the clinical trial.
Prerequisites: FDA IDE approval, IRB, and NIWC HRPO approval.
Materials & Dependencies: None
Milestone: (MAC47) First subject enrolled in (b)(4) study.
Deliverable: Documentation of treatment of first subject using (b)(4) system.

3.6 Clinical trial management
Goal: To ensure a successful completion of the clinical trial (MAC43-MAC60)
Strategy: As study Sponsor, the contractor is accountable for the overall success of the human trial. This includes responsibility for site training, compliance including proper documentation, data collection processes, data analysis and management, and ensuring successful completion and write-up the clinical trial.
Prerequisites: FDA IDE approval, IRB, and NIWC HRPO approval.
Materials & Dependencies: None
Milestone: (MAC59) Three subjects treated using (b)(4) system.
Deliverable: Clinical trial report.

Tasks 3.5 and 3.6 contain Human Subject Research (HSR). Work shall not proceed until IRB protocols have been approved, and NIWC HRPO approval letter has been received by contractor.

DARPA Review

3.7 Phase 3 demonstration and report (MAC60)
Prepare phase 3 clinical demonstration of the fully (b)(4) system
Goal: To demonstrate the successful completion of the contract
Strategy: Prepare documentations for phase 3 demonstration
Prerequisites: None
Materials & Dependencies: None
Milestone: (MAC60) Phase 3 clinical demonstration and report are completed

Deliverable: Phase 3 final report

5.0 Milestones

Milestones highlighted green contain HSR.

Task	Description	MAC
Technical Phase 1		
1.1	**Institutional IACUC approval and DOD ACURO review**	
1.1.1	Protocols approved by University of Pittsburgh IACUC committee	1
1.1.2	Protocol review completed by DOD ACURO	2
1.2	**Animal studies to develop the external system and the(b)(4) system**	
1.2.1	**Restore bladder function**	
1.2.1.1	Pudendal nerve block by(b)(4) is achieved in 2 cats. Pudendal nerve block is measured as urethral pressure <5 cmH2O	3
1.2.1.2	Low pressure (<50 cmH2O) voiding is induced in 2 cats	4
1.2.1.3	Number of animals is 4 for low pressure voiding to achieve statistically significant results	5
1.2.1.4	Number of animals is 6 for low pressure voiding to achieve statistical significance	6
1.2.2.1	Restoring defecation in 2 cats by 3 pudendal nerve(b)(4) If successful, the stimulation method shall be tested in all other cats. Defecation is measured by increase in colon pressure and elimination of the balloon catheter from the distal colon	7
1.2.2	**Restore bowel function**	
1.2.2.2	Restoring defecation in 2 cats by 2 pudendal nerve(b)(4) and 1 sacral root(b)(4) If successful, the stimulation method will be tested in all other cats.	8
1.2.2.3	Restoring defecation in 2 cats by 2 pudendal nerve(b)(4) in combination with(b)(4) of sacral spinal cord. If successful, the stimulation method will be tested in all other cats	9
1.2.2.4	Complete the last 2 cats in 1.2.2 to achieve statistical significance	10
1.2.3	**Restore sexual function**	
1.2.3.1	Restoring penile erection in 2 cats by 1 pudendal nerve(b)(4) If successful, the stimulation method will be tested in all other cats. If not successful, the milestones 1.2.3.2-1.2.3.4 shall be performed as planned.	11

1.2.3.2	Restoring penile erection in 2 cats by 1 pudendal nerve(b)(4) and 1 sacral root(b)(4) If successful, the stimulation method shall be tested in all other cats.	12
1.2.3.3	Restoring penile erection in 2 cats by 1 pudendal nerve(b)(4) in combination with magnetic stimulation of sacral spinal cord. If successful, the stimulation method shall be tested in all other cats	13
1.2.3.4	Complete the last 2 cats in 1.2.3 to achieve statistical significance	14
1.2.4	**Measure fullness of bladder and bowel**	
1.2.4.1	Recording pelvic nerve activity in 2 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is if the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.	15
1.2.4.2	Recording pudendal nerve activity in 2 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.	16
1.2.4.3	Recording both pudendal and pelvic nerve activity in 4 cats. The amplitude and frequency of nerve activity shall be monitored. If a correlation between an increase in the amplitude and/or frequency of the nerve activity and the bladder/blow fullness can be established, this study shall be counted as a success. Criteria for success is for the bladder/bowel fullness can be correctly detected by increase in nerve activity in >90% of the times.	17
1.2.5	**Test(b)(4) and device prototypes**	
1.2.5.1	First prototypes of animal leads/cuffs are tested to confirm the impedance is less than 1k ohm and the size/length is appropriate for cats.	5
1.2.5.2	First prototype of the test bed environment is tested to confirm that it can generate the stimulation signals as designed	4
1.2.5.3	First version(b)(4) is tested to confirm its functionality	11
1.2.5.4	First prototypes of human(b)(4) are tested to confirm the impedance is less than(b)(4)	12

(b)(4)	1.2.5.5	Wireless charging is tested to confirm its function	10
(b)(4)	1.2.5.6	Wireless communication antenna is tested for selection	9
	1.2.5.7	The (b)(4) and device prototype designs are finalized	15
	1.3	**Test Bed Environment for both (b)(4) Systems**	
	1.3.1	Complete initial schematic design with design review	2
(b)(4)	1.3.2	Complete initial board layout, fabrication/assembly and evaluation	3
	1.3.3	PC test application with (b)(4) connectivity (potentially wired or BLE depending on final requirements)	4
	1.3.4	Integration of in enclosure with firmware and PC application connectivity	4
	1.4	**(b)(4) for animal study (Version 0)**	
	1.4.1	(b)(4) design with design review complete	6
	1.4.2	Can samples developed and fully evaluated (b)(4)	9
	1.4.3	(b)(4)	10
	1.4.4	Final PC test application with (b)(4) connectivity	9
	1.4.5	Full integration and test completed for initial prototype	11
	1.5	**Stimulation (b)(4) for animal studies**	
	1.5.1	Finalize on the (b)(4) and length	2
	1.5.2	Finalize design of (b)(4)	3
	1.5.3	First prototypes of (b)(4) delivered for test	5
	1.5.4	Finalize design and (b)(4) electrode production	7
	1.6	**(b)(4) for human study**	
	1.6.1	Industrial design and (b)(4) for the custom enclosure	8
	1.6.2	Integration of the (b)(4) components with firmware and the enclosure	10
	1.6.3	System verification completed	15
	1.6.4	Documentation supporting the IDE submission	15
	1.6.5	Build 8 sets of (b)(system to conduct GLP safety study in 4 pigs in Phase 1.	14
(b)(4)	**1.7**	**(b)(4) for human use**	
	1.7.1	Finalize on the (b)(4 size and length	4
	1.7.2	Finalize design of human (b)(4	8
	1.7.3	First prototypes of (b)(4 delivered for test	12
	1.7.4	Finalize design and production	15
	1.7.5	Biocompatibility test is completed. Documentations for FDA IDE submission	15
	1.8	**Physician/Investigator controller for human (b)(4 and animal (b)(4**	
	1.8.1	Schematic design complete	9
	1.8.2	Evaluation (b)(4) assembled and initial evaluation complete	11

1.8.3	Integration with a simple enclosure with display and firmware	12
1.8.4	Final documentation to support the FDA IDE as an accessory device	15
1.9	**Patient controller for human(b)(4)**	
1.9.1	Firmware features complete to restrict use as a patient controller	12
1.9.2	Verification testing completed	13
1.10	**Software Development Kit**	
1.10.1	Requirements understood for SDK	6
1.10.2	At the completion of the development, the SDK is complete with the documentation on how to access the devices via the software API	15
1.11	**GLP animal study**	
1.11.1	GLP safety study is completed for the external system	15
1.12	**Human cadaver study**	
1.12.1	Cadaver study is completed with a total of 3 cadavers	10
1.13	**Early feasibility human clinical protocol for system**	
1.13.1	Human clinical protocol is ready for inclusion in pre-submission to FDA.	15
1.14	**FDA IDE pre-submission #1**	
1.14.1	FDA IDE pre-submission #1 is sent to FDA for the external stimulation system	3
1.14.2	FDA IDE pre-submission #1 meeting is completed for the external stimulation system.	5
1.15	**FDA IDE pre-submission #2**	
1.15.1	FDA IDE pre-submission #2 is sent to FDA for the external stimulation system	8
1.15.2	FDA IDE pre-submission #2 meeting is completed for the external stimulation system.	10
1.16	**FDA IDE submission**	
1.16.1	FDA IDE application for the external stimulation system is submitted	15
1.16.2	IDE approved by FDA for the external stimulation system	18
1.17	**DARPA Preliminary Design Review**	
1.17.1	DARPA preliminary design review is completed	12
1.18	**DARPA Critical Design Review**	
1.18.1	DARPA critical design review is completed	15
1.19	**Final demonstration and report**	
19.1.1	Phase 1 final demonstration and report are completed	18
Technical Phase 2		
2.1	**Non-GLP animal study using the(b)(4) system**	
2.1.1	Non-GLP animal study in normal cats	
2.1.1.1	Version #1 is tested in 2 cats	22

(b)(4)

(b)(4)

2.1.1.2	Improved version (b)(4) is tested in 2 cats	24
2.1.1.3	Improved version is tested in 2 cats	26
2.1.1.4	Improved version is tested in 2 cats	27
2.1.2	Non-GLP animal study in awake SCI cats	
2.1.2.1	Version (b)(4) is tested in 2 cats	31
2.1.2.2	Improved version (b)(4) is tested in 2 cats	34
2.1.2.3	Improved version is tested in 2 cats	37
2.1.2.4	Improved version is tested in 2 cats	39
2.2	**IRB approval and NIWC HRPO approval for human studies using the external stimulation**	
2.2.1	Protocols approved by University of Pittsburgh IRB committee	19
2.2.2	Protocol review completed by NIWC HRPO	20
2.3	**Early feasibility study in human SCI subjects using the external stimulation system**	
2.3.1	First human subject is enrolled	30
2.3.2	Human clinical study is completed with 3 SCI subjects tested	42
2.4	**(b)(4) with Custom (b)(4) for Animal Study (Version 1/2)**	
2.4.1	Update to Version – to meet any new requirements and/or fix issues found during animal testing in Phase –	27
2.4.2	Build 8 sets of the version – and improved version (b)(4) system for testing in 8 anesthetized cats	27
2.4.3	Update to Version – to meet any new requirements and/or fix issues found during the continuing animal studies in Phase 2	27
2.5	**2.5 (b)(4) (Support Animal Trials and IDE Human Use)**	
2.5.1	Update (b)(4) Design with Design Review Complete	23
2.5.2	samples developed and fully evaluated (b)(4) (b)(4)	25
2.5.3	(b)(4)	27
2.5.4	Complete longevity study; the contractor shall use prediction tools to evaluate the reliability of the electronics at the expected stress levels. (b)(4) longevity will be supplied by the chosen (b)(4) manufacturer. Completion of accelerated life testing.	28
2.5.5	Full Integration and test completed for initial prototype	31
2.5.6	Biocompatibility test is completed	31
2.5.7	Human (b)(4) development is completed and documentations are ready for FDA IDE submission.	31
2.6	(b)(4)	
2.6.1	First units are tested and documentation updated to support the FDA IDE submission; three units are planned	21

2.6.2	Units are upgraded for new requirements to support additional configurations (software only)	29
2.7	(b)(4)	
2.7.1	Firmware updates to support the latest patient configurations	23
2.7.2	Second iteration of firmware updates to support the latest patient configurations	30
2.8	(b)(4) **for Human Study**	
2.8.1	Complete software iteration to support the latest requirements coming from the research team.	25
2.9	**GLP animal study**	
2.9.1	GLP safety study is completed for the (b)(4) system	39
2.10	**Human cadaver study**	
2.10.1	Cadaver study is completed with a total of 3 cadavers	23
2.11	**Early feasibility human clinical protocol for (b)(4) system**	
2.11.1	Human clinical protocol is ready for inclusion in pre-submission to FDA.	26
2.12	**FDA IDE pre-submissions #1 for the (b)(4)**	
2.12.1	FDA IDE pre-submission #1 is completed for the (b)(4)	20
2.12.2	FDA IDE pre-submission #1 meeting is completed for the (b)(4) system	22
2.13	**FDA IDE pre-submissions #2 for the (b)(4) system**	
2.13.1	FDA IDE pre-submission #2 is completed for the (b)(4) system	26
2.13.2	FDA IDE pre-submission #2 meeting is completed for the (b)(4) system	28
2.14	**FDA IDE pre-submissions #3 for the (b)(4) system**	
2.14.1	FDA IDE pre-submission #3 is completed for the (b)(4) system	35
2.14.2	FDA IDE pre-submission #3 meeting is completed for the (b)(4) system	37
2.15	**FDA IDE submission for (b)(4) system**	
2.15.1	FDA IDE application for the (b)(4) system is submitted	39
2.15.2	IDE approved by FDA for the (b)(4) system	42
2.16	**Clinical trial preparations and enrollment**	
2.16.1	First subject enrolled in study	30
2.17	**Clinical trial management**	
2.17.1	Three subjects treated using system	42
2.18	**Phase 2 demonstration and report**	
2.18.1	Phase 2 animal demonstration and report are completed	42
2.18.2	Phase 2 clinical demonstration and report are completed	42

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Technical Phase 3		
3.1	**3.1 IRB approval and NIWC HRPO approval for human studies using the implantable system**	
3.1.1	Protocols approved by IRB committee	43
3.1.2	Protocol review completed by NIWC HRPO	44
3.2	**Early feasibility study in human SCI subjects using the (b)(4) system**	
3.2.1	First human subject is enrolled	47
3.2.2	Human clinical study is completed with 3 SCI subjects tested	59
3.3	**(b)(4) for Human Use**	
3.3.1	Build 9 sets of the FDA IDE approved system for testing in human studies	47
3.3.2	Provide device support and update devices or build new ones depending on the requested changes to support the research team. Any updates made that affect the requirements or potential risk shall be updated. For verification of updates, the engineering team with the regulatory team shall decide what type of testing is needed (full re-run of verification vs regression) and then testing shall be executed with the proper reports.	59
3.4	**(b)(4)**	
3.4.1	Build 9 sets of the FDA IDE approved system for testing in human studies	47
3.4.2	Provide device support and update devices or build new ones depending on the requested changes to support the research team. Any updates made that affect the requirements or potential risk shall be updated. For verification of updates, the engineering team with the regulatory team shall decide what type of testing is needed (full re-run of verification vs regression) and then testing shall be executed with the proper reports.	59
3.5	**Clinical trial preparations and enrollment**	
3.5.1	First subject enrolled in study	47
3.6	**Clinical trial management**	
3.6.1	Three subjects treated using system	59
3.7	**Phase 3 demonstration and report**	
3.7.1	Phase 3 clinical demonstration and report are completed	59

6.0 Deliverables

Task	Description	MAC
Technical Phase 1		
1.1.1	Approved IACUC protocols	1

1.1.2	DOD ACURO approval letter	2
1.2.1	Animal experiment data/results for bladder function	6
1.2.2	Animal experiment data/results for bowel function. Bowel function is restored in anesthetized SCI cats by 3(b)(4) on the pudendal nerves, or by(b)(4) on the pudendal nerves and(b)(4) on sacral root, or by(b)(4) nerves combined with spinal cord (b)(4)	10
1.2.3	Animal experiment data/results for sexual functions. Penile erection or vaginal contraction/lubrication is restored in chronic SCI cats by(b)(4) (b)(4) on the pudendal nerve, or by(b)(4) on the pudendal nerve and(b)(4) on sacral root, or by(b)(4) (b)(4) combined with(b)(4) (b)(4)	14
1.2.4	Animal experiment data/result for detecting bladder and bowel fullness	17
1.2.5	Animal experiment data/results from the tests of the(b)(4) and device prototypes	15
1.3	A prototype unit for early animal research. Two set of the prototypes will be provided at MAC4 for the tasks 1.2	4
1.4	Provide 5 sets of version(b)(4) to test in anesthetized normal/SCI cats in phase 1. The version is the first prototype of the which has included all(b)(4) as determined by the task 1.2 to restore bladder, bowel, and sexual functions.	11
1.5	Provide(b)(4) developed	7
1.6.1	Documentation and device are ready for IDE submission	15
1.6.2	Provide 8 sets of system to conduct GLP safety study in 4 pigs in Phase 1. Four sets will be tested, and 4 sets will be used as backup in case that replacements are needed	15
1.7	Provide(b)(4) for each(b)(4) developed. Provide documentations for(b)(4) IDE submission.	15
1.8	(b)(4) meets the requirements to control the IPG to support the animal studies and for human study with FDA IDE for(b)(4	15
1.9	(b)(4) meets the requirements to control the for human use to support the IDE study for Phase 2.	13
1.10	Source Code, Library and documentation for the SDK	15
1.11	GLP safety study data for the(b)(4) system and related documentation for FDA IDE submission	15
1.12	Documentation for surgical approach and the design documentation of the insertion tools for the external system	10
1.13	Complete early feasibility clinical study protocol.	15
1.14.2	FDA IDE pre-submission #1 documentation for the(b)(4) system and all related FDA communications	3
1.14.2	FDA IDE pre-submission #1 meeting documentation for the(b)(4) (b)(4) system and all related FDA communication	5

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1.15.2	FDA IDE pre-submission #2 documentation for the (b)(4) system and all related FDA communications	8
1.15.2	FDA IDE pre-submission #2 meeting documentation for the (b)(4) (b)(4) system and all related FDA communication	10
1.16.1	FDA IDE submission for the (b)(4) system and all related FDA communication	15
1.16.2	FDA IDE approval for the (b)(4) system and all related FDA communication	18
1.17	Preliminary design documentation	12
1.18	Phase 1 system design documentation	15
1.19	Phase 1 final report	18
Technical Phase 2		
2.1.1	Animal experiment data/results for the version of the (b)(4) system	27
2.1.2	Animal experiment data/results for the version of the (b)(4) system	39
2.2.1	Approved IRB protocols	19
2.2.2	NIWC HRPO approval letter	20
2.3.1	First human subject enrollment documentation	30
2.3.2	Data and documentation of early feasibility study of the (b)(4) stimulation system	42
2.4.2	Provide 8 sets of the version #1 and/or improved version #1 (b)(4) system for testing in 8 anesthetized cats	27
2.4.3	Version 2 for testing in awake chronic SCI cats	27
2.5.4	Build 16 sets of the version (b)(4) system for testing in 8 awake SCI cats.	28
2.5	Build 16 sets of the (b)(4) version (b)(4) system to conduct safety GLP studies of 8 awake pigs. Provide documentations for FDA IDE submission.	31
2.6	Provide 3 (b)(4) with supporting documentation to support an FDA IDE submission and the ongoing animal trials and for the human clinical in Phase 3	29
2.7	Build 9 (b)(4) units to support each of the human devices for Phase 3	30
2.8	Build 9 sets of the FDA IDE approved (b)(4) system for testing in human studies	25
2.9	GLP safety study data for the (b)(4) system and related documentation for FDA IDE submission	39
2.10	Documentation of surgical approach and design documentation of (b)(4) tools for the (b)(4) system	23
2.11	Complete feasibility clinical study protocol	26
2.12.1	FDA IDE pre-submission #1 documentation for the (b)(4) system and all related FDA communication	20
2.12.2	FDA IDE pre-submission #1 meeting documentation for the (b)(4) system and all related FDA communication	22

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2.13.1	FDA IDE pre-submission #2 documentation for the (b)(4) system and all related FDA communication	26
2.13.2	FDA IDE pre-submission #2 meeting documentation for the (b)(4) system and all related FDA communication	28
2.14.1	FDA IDE pre-submission #3 documentation for the (b)(4) system and all related FDA communication	35
2.14.2	FDA IDE pre-submission #3 meeting documentation for the (b)(4) system and all related FDA communication	37
2.15.1	FDA IDE submission for the (b)(4) system and all related FDA communication	39
2.15.2	FDA IDE approval for the (b)(4) system and all related FDA communication	42
2.16	Documentation of treatment of first subject using system	30
2.17	Clinical trial report	42
2.18	Phase 2 Final Report	42
Technical Phase 3		
3.1.1	Approved IRB protocols	43
3.1.2	NIWC HRPO approval letter	44
3.2.1	First human subject enrollment documentation	47
3.2.2	Human clinical study is completed with 3 SCI subjects tested	59
3.3.1	Provide 9 sets of the FDA IDE approved system for testing in human studies	47
3.3.2	Updated devices as required.	59
3.4.1	Provide 9 sets of the FDA IDE approved system for testing in human studies	47
3.4.2	Updated devices as required.	59

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7.0 Program Management and Review

The Government shall work alongside the performer to ensure performed tasking is in sync and matched with the research goals. With the Government Technical Representative (GTR), the recipient shall collaborate and cooperate with other DARPA performers within the program. Demonstration scenarios and parameters shall be reviewed and discussed between the GTR and the Recipient prior to the event. The Government shall participate in critical technical and design reviews and discussions via monthly teleconferences with the DARPA sponsor and the Contractor. Under direction of the Government, the Contractor shall collaborate and cooperate with other performers in the program. At the Principal Investigator (PI) meetings, the Government shall ensure all performers demonstrate their technical capabilities and engage each other in cooperative yet challenging environment. The Government shall ensure that the performers each share technical information with each other, as appropriate, to enable the testing and challenging of each other's capabilities. Additionally, the Government and Recipient shall review and discuss proposed press releases that reference DARPA, the Department of Defense, or this agreement (excluding peer reviewed publications of scientific findings) prior to release.

Academic recipients considered to be conducting fundamental research on this program may publish papers describing scientific or engineering advances that are general in nature and adhere to the above guidance. The Contractor shall submit any publications to the DARPA Program Manager for pre-publication review. Should the character of the research change during award performance so that the research is no longer considered fundamental, the award shall be modified to impose the restrictions on public release and dissemination of information that apply to those research efforts that are not considered fundamental research. Non-academic performers shall submit any publications to DARPA's Public Release Center (DARPA/PRC) to process for pre-publication review.

Kick-off Meeting

The contractor shall hold a kick off meeting within 60 days of award of this contract. In this meeting, the contractor shall present a program management plan and financial tracking plan. Presentation materials for this meeting shall be provided to the Government.

Monthly Financial Reports

The contractor shall provide monthly financial progress reports to NIWC PACIFIC and DARPA. The financial report shall provide a breakout of invoiced expenditures for the month.

Quarterly Technical Reporting

The contractor shall provide quarterly progress reports to NIWC PACIFIC and DARPA. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, present any specific data reports outlined in sow for that quarter, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work.

Monthly Teleconference

The contractor shall participate in a regular teleconference meetings to maintain communications with the Government team. The purpose of the technical update is to provide a brief project progress and inform DARPA Program Manager of any potential issues.

Semi-annual Principal Investigator (PI) Meetings

The contractor shall participate in the following program-wide meetings:

- Phase I Kick-off (Month 1) [DARPA]
- Phase II Kick-off (Month 1 of Phase II) [DARPA]
- Phase II mid-Phase Technical Interchange Meeting (TIM) (Month 12 of Phase II)
- Phase III Kick-off (Month 1 of Phase III)
- Phase III mid-Phase Technical Interchange Meeting (TIM) (Month 12 of Phase III)

The purpose of these reviews is to present a summary of work completed and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. The semi-annual meetings shall also be used for coordination with the other members of the BG plus program and to perform integration demonstrations.

Final Contract Review
The recipient shall provide a final contract review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. A final contract summary report shall be provided to NIWC PAC and DARPA at the end of the program.

8.0 Travel

Travel is anticipated for the program kickoff meeting, semi-annual PI meetings, meetings with collaborators, and meetings with DARPA

9.0 Place of Performance

The work shall be performed at the contractor and subcontractor facilities.

10.0 Technical POC's

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