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Award Number: W81XWH-08-1-0419

TITLE: Clinical Phase IIB Trial of Oxycyte Perflurocarbon in Severe Human Traumatic Brain Injury

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REPORT DATE: October 2011

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01-10-2011	Annual	2 SEP 2010 -1 SEP 2011

4. TITLE AND SUBTITLE
Clinical Phase IIB Trial of Oxycyte Perflurocarbon in Severe Human Traumatic Brain Injury

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-08-1-0419

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Miami
Miami, FL 33101

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

In October of 2010, the Principal Investigator of this DOD funded award traveled to Ft. Detrick, Maryland and gave a presentation to 12 members of the CDMRP staff concerning the status of the project with perfluorocarbons in severe human traumatic brain injury. The project was placed on hold, based upon a decision by the Food and Drug Administration not to allow a clinical trial with the perfluorocarbon oxycyte to be performed within the United States. In accordance with FDA recommendations, however, Oxygen BioTherapeutics, the company that manufactures oxycyte, performed a dose escalation clinical trial in Switzerland and Israel and the first batch of results in the first cohort of patients was obtained and proved to be satisfactory. Based upon these facts, and on the recommendation of the scientific program officer in the DOD, Dr. Charmaine Richmond, a request for a no cost extension to this project was submitted. A revised statement of work was also submitted, effectively changing the project from a human clinical trial to an animal study.

15. SUBJECT TERMS
TBI, perfluorocarbons, traumatic brain injury

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	6	19b. TELEPHONE NUMBER *(include area code)*

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Annual Progress Report

DOD Grant #PT074521W81XWH-08-1-0419-October 1st, 2011

Principle Investigator: Bullock, R.

Introduction and grant rationale

Perfluorocarbons are one of the methods by which oxygen delivery to tissue can be achieved after injury. Neurological injury [brain and cord] is always accompanied by tissue ischemia/hypoxia and much of the damage seems to be mediated by this secondary mechanism. The rationale for perfluorocarbons in traumatic brain injury has been well established in our animal studies and early phase 2 trials. Currently three perfluorocarbons are available in the United States for testing, but none of these have been FDA approved and only for one of them – oxycyte has the process of application for FDA approval even been commenced.

For the third generation perfluorocarbon (oxycyte) a possible side effect that has emerged in humans is transient mild thrombocytopenia. It is uncertain at this time whether this side effect will prove to be a limiting factor which may jeopardize the use of these compounds as a class, or just affect oxycyte in particular following traumatic brain and spinal cord injury. Any agent which might exacerbate thrombocytopenia in intracranial hemorrhage into traumatic contusions could, for obvious reasons be dangerous. The purpose of this grant therefore is to cross compare the safety and efficacy of three perfluorocarbons namely oxycyte, perftoran and oxygent. The letter of award was made in August [appendix 1] and in this first quarterly report we outline progress that has been made in the two month period since the award notice was received.

Body:

The above captioned CDMRP Award was made for a randomized clinical trial of the perfluorocarbon oxycyte an oxygen carrier, in severe traumatic brain injury. Please see previous interim reports relevant to this study. Although at the time the application was made to the CDMRP, the FDA had issued an IND for trials of oxy site in traumatic brain injury, they placed a clinical hold on this phase II B trial in late 2008, and at an appeal meeting in October 2008 this hold was continued based upon the position that there was a risk of thrombocytopenia with perfluorocarbons in general. Consequently, the CDMRP funds were placed into Escrow and the company, Oxygen Biotherapeutics raised venture capital funding to support a Phase II trial in Europe to demonstrate the safety of oxycyte to the Food and Drug administration. This trial [named "Stop TBI"] was designed to comply with suggestions provided by the FDA. The trial was designed to enroll 128 patients in the following centers.

Switzerland;

1- University Hospital of Geneva
2- University Clinic for Neurosurgery Inselspital Bern
3- Neurosurgical Clinic Kantonspital Aarau
4 Poly Clinic for Neurosurgery University Hospital Basel
5 Intensive Care Medicine University Hospital Zurich.

Centers in Israel;

1- Hadassah Medical Center
2- Ramban Health Center
3- Sheba Medical Center
4- Sourasky Medical Center
5- Soroka Medical Center.

In addition, the University of Singapore is currently in negotiations with the company to enroll in the trial.

Conclusion

During 2010, Col Dallas Hack, MD, head of the CDMRP program, requested the PI to provide a powerpoint briefing, at FT Detrick, MD, on the topic of the role of Perfluorocarbons, in Traumatic Brain Injury. Dr Dwayne Tagliaferro was assigned as scientific review/program officer for the project.

For this briefing, the PI was instructed to present the case for evaluating an alternative PFC, namely PERFTEC, (PERFTORAN) a Russian made PFC, used in Mexico, and a few other countries, but not yet FDA approved in USA. For this information, the PI had multiple calls with Gen Jack Woodmansee, and representatives of Laboratorios KEM, in Tijuana, Mexico.

Col Hack requested an assessment of the 3 available PFC's in the USA in several TBI models.

The Letter of intent, and finally the grant, were approved, and awarded, in July 2011, subject to responding to reviewers' comments which were completed by august 2011.