

Wayne State Warriors Marijuana Clinical Research Program: Investigating the Impact of Cannabinoids on Veterans' Behavioral Health

Leslie H. Lundahl, PhD, Lead Principal Investigator
David Ledgerwood, PhD, Co-Principal Investigator

Project Aims:

In this randomized, controlled clinical trial we are recruiting veterans with PTSD who report using cannabis. **We are conducting two studies that are complementary and linked via their aims and methodology.** In **Study 1**, 200 veterans will be randomized into one of four different THC:CBD dose conditions (THC; CBD; THC+CBD, and placebo) for a 12-week treatment phase. In **Study 2**, 150 veterans will be randomized into *one of two groups*: a THC reduction group (n=75), tailored across THC products that are approximately 50% lower in THC than the products participants currently use; or a THC reduction + 1:1 THC:CBD group (n=75), also including tailored THC concentrations as in the first group but with CBD added in a 1:1 THC:CBD ratio. Within each Study 2 treatment group, participants will be randomly assigned on a 1:1 basis to either start the 12-week treatment after a 2-week baseline or a 6-week baseline so we can examine participant naturalistic cannabis use before introducing the new product. **Both studies** involve assessments weekly and bi-weekly throughout a 12-week treatment phase, and at 3- (post-treatment), 6-, 9, and 12-months post-baseline. **Primary outcomes** include clinical assessments of PTSD symptom severity, mood and anxiety symptoms, and suicidality. **Secondary measures** include (1) neurocognitive function; (2) overall health, sleep quality, pain, healthcare utilization, and quality of life; (3) individual differences in fear learning and extinction associated with PTSD symptom severity; (4) saliva for DNA analysis to examine genetic and epigenetic markers associated with the endocannabinoid system; and, (5) urine, blood, and saliva samples to quantify levels of endocannabinoids and their metabolites (e.g., anandamide [AEA] and 2-AG), as well as THC and CBD and their metabolites, to examine whether these levels vary as a function of THC:CBD dose mixtures and differentially affect outcomes. Data will be analyzed to determine which dose conditions might be associated with the outcome measures. These data will be used to (1) develop a predictive algorithm that will help determine personalized profiles of patients who may be at increased risk for suicide; and, (2) develop a profile of who might most benefit from cannabinoid therapeutics.

1). Project Milestones

Study 1 and Study 2 Protocols have been revised and finalized in accordance with discussion with CRA/LARA.

- **Project Progress**

Based on feedback from the Michigan Department of Military and Veterans Affairs (DMVA), we revised our advertising materials to be sent out to veterans in surrounding counties and updated the brochures that will be distributed at job fairs and events. We will send these materials to the DMVA for feedback prior to submitting them to our IRB for approval. We continue to update our project website (www.warriorCARE.net) regularly. Our studies are also listed on ClinicalTrials.gov, which also provides contact information to enhance referral efforts.

Our full-time recruiter continues to maintain contact with Veteran-related organizations we can approach for referrals and events like job fairs, where we can rent exhibition booths for our research staff to answer questions, provide information, conduct initial screening interviews and schedule in-

person screening. We also continue to check in with the Veterans on our waitlist, ensuring we can ramp up recruitment quickly once all regulatory requirements are completed.

We have received CoA results for one cannabis plant material strain from the irradiation and testing processes NIDA is conducting on the cannabis bulk stocks. We are still awaiting the CoA results from two more strains which we should have by the end of the month. Once we have received all three CoA reports we will file the FDA IND application listing NIDA Drug Supply Program as the source.

The DEA Schedule I Protocols for both studies have been completed and will be submitted to the DEA for approval when we submit the INDs applications to the FDA.

• Noteworthy Accomplishments – Identify and describe any milestones reached or noteworthy accomplishments completed during the period.

The revised Study 2 (TRS) protocol has been resubmitted to the Wayne State University Institutional Review Board to address minor changes required by that board, and we anticipate receiving final IRB approval soon. We are also continuing our ongoing edits of regulatory documentation, including updating our clinicaltrial.gov entries for this project, and we have started preparing an IRB amendment to address minor changes to consent forms and questionnaires.

The WarriorCARE van is being equipped for phlebotomy and physiological monitoring during home visits during the clinical trial.

Research staff is continuing to train on all procedures.

2). Delays – Brief description of problems or delays, real or anticipated, which should be brought to the attention of the Grant Administrator.

While we await final IRB approval for Study 2 protocol changes and for DEA-approved research cannabis products to become available, we continue to operate under reduced salary support for research staff members.

3). Statement concerning any significant deviation from previously agreed-upon Statement of Work.

N/A

4). Financial expenditures of grant money and other contributions to the project, in-kind and/or direct funding.

Wayne State University: Veteran Marijuana Research 2021 Grant
Title: Investigating the Impact of Cannabinoids on Veterans' Behavioral Health

CATEGORY	TOTAL BUDGET	Expenses-thru 12/31/23	% of Budget Spent
Personnel/Fringe	3,925,223	1,070,822	
Equipment	129,404	58,684	
Supplies/Other	2,282,480	186,958	
Computers	45,575	9,321	
Travel	-	-	
DIRECT TOTALS	6,382,682	1,325,785	20.77%
Indirect Costs- 10%	638,268	132,579	
BUDGET TOTALS	7,020,950	1,458,364	20.77%

Attachments and Other Materials – Provide project materials developed and implemented during the reporting period (e.g. newspaper articles, newspaper advertisements, forms, brochures, announcements, studies, reports, analyses, audits, etc.).”

N/A

Respectfully submitted,



Leslie H. Lundahl, PhD
 Lead/Contact Principal Investigator



David M. Ledgerwood, PhD
 Co-Principal Investigator

January 10, 2024



Sponsored Program Administration
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FINANCIAL STATEMENT

Agency State of Michigan Dept of Licensing & Regulation	WSU Index No. 370718M & 380156SUB	Report Period 10/01/23 Thru 12/31/23		Date 01/12/24
Title: Veterans Marijuana Research 2021	Grant Code 23T1C	Fund Code: 23T1C1	Project Period 08/16/21 Thru 07/31/24	
Principal Investigator Dr. Leslie H. Lundahl	Final NO	Org. Code: 06CMN1	Reporting No. 7	
			Grant/Contract No. VMR202101	

CATEGORY	EXPENDITURES		AGREEMENT	
	Current Period	Cumulative	Budget	Balance
Salaries & Wages	\$33,043.67	\$840,525.25	\$3,080,771.00	\$2,240,245.75
Fringe Benefits	\$9,615.59	\$230,297.45	\$844,452.00	\$614,154.55
Travel	\$40.61	\$40.61	\$0.00	(\$40.61)
Supplies & Materials	\$27,196.35	\$67,275.66	\$2,328,055.00	\$2,280,779.34
General Expenses	\$0.00	\$0.00	\$0.00	\$0.00
Equipment	(\$20,965.44)	\$58,684.44	\$129,404.00	\$70,719.56
Tuition	\$0.00	\$0.00	\$0.00	\$0.00
ROUNDING				
TOTAL DIRECT	\$48,930.78	\$1,196,823.41	\$6,382,682.00	\$5,185,858.59
Indirect Costs Rate: 10.00%	\$4,893.07	119,682.35	\$638,268.00	\$518,585.65
TOTAL EXPENDITURES	\$53,823.85	\$1,316,505.76	\$7,020,950.00	\$5,704,444.24

STATUS OF REVENUE		OUTSTANDING INVOICES	
Previously Reported	\$1,262,681.01	Date	Invoice No. Amount
Current Billing	\$53,823.85		
Total Expenditures	\$1,316,505.76		
Total Payments to Date	\$3,510,475.00		
Outstanding Amount	(\$2,193,989.24)		
outstanding			
		Total	\$0.00

CERTIFICATION: BY SIGNING THIS REPORT, I CERTIFY TO THE BEST OF MY KNOWLEDGE AND BELIEF THAT THE REPORT IS TRUE, COMPLETE, AND ACCURATE, AND THE EXPENDITURES, DISBURSEMENTS, AND CASH RECEIPTS ARE FOR THE PURPOSES AND INTENT SET FORTH IN THE AWARD DOCUMENTS. I AM AWARE THAT ANY FALSE, FICTITIOUS, OR FRAUDULENT INFORMATION MAY SUBJECT ME TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES (U.S. CODE, TITLE 18, SECTION 1001)

NAME: *Marlene Emo* Senior Director of Sponsored Program Administration *for* DATE: *1/12/24*