

**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**

During this period we continued our communication with Veterans organizations and have been invited to meet with the behavioral health treatment team at the Detroit VA to recruit participants. We continued to reach out to veteran organizations through Facebook and contacted coordinators from other veteran organizations to keep them apprised of our readiness to recruit. Our recruitment team is working with Wayne State University Veteran organizations, including the Office of Military & Veterans Academic Excellence. We update our project website ([www.warriorCARE.net](http://www.warriorCARE.net)) regularly. Our studies are also listed on ClinicalTrials.gov, which provides contact information, as well.

Our full-time recruiter continues to seek out 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, conducting initial screening interviews and schedule in-person screening. We are maintaining a waitlist of Veterans who express interest in participating, ensuring we can ramp up recruitment quickly once all regulatory requirements are completed.

We changed our cannabis dosing procedure to be consistent with NIH/NIDA recommendations to use a standard treatment unit (STU: 5 mg THC) in human cannabis research, so we now have more flexibility with the flower products we can use. This means that we can use cannabis flower from the NIDA Drug Supply Program (NDSP). Although we will need greater quantities than they likely can supply, they believe they can provide enough for at least the first year. This will allow us to get started (i.e., complete approximately 60 participants) and also gives our other DEA-approved grower time to produce flower for the remainder of the study. We are confident that between the two, we will be able to obtain the cannabis needed to complete the studies. Thus we are submitting two separate INDs (one for each supplier). We are currently waiting on the Letter of Authorization from NIDA that allows us to reference their DMF that must accompany the IND request. For the second grower, the WSU legal department is currently reviewing an NDA and Letter of Intent from the grower. Once those are executed, we can submit the IND with them so they can provide cannabis for us.

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.

The ClinCard system for participant payments for both studies has been established.

Screening visit safety checklists for both studies have been created and staff has been trained on all procedures.

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

The revised Study 1 (CBH) protocol has received Psychiatry Department Review Board and Wayne State University Institution Review Board approval.

The Supplemental Brain Imaging Study team has integrated the MRI protocol into Study 1 which now has IRB approval.

The revised Study 2 (TRS) protocol has received Psychiatry Department Review Board approval and is currently under review at the Wayne State University Institution Review Board.

The mobile pharmacology van has been delivered. We are currently awaiting installation of WarriorCARE logo decals, locking safe (to store cannabis being delivered), and shelving units for equipment. This van will allow us to deliver cannabis doses and conduct assessments at participant's homes which will be more convenient for veterans who may have transportation/mobility issues.

**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 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**

<b>CATEGORY</b>	<b>TOTAL BUDGET</b>	<b>Expenses-thru 3/31/23</b>	<b>% of Budget Spent</b>
Personnel/Fringe	3,925,223	901,522	
Equipment	129,404	79,650	
Supplies/Other	2,282,480	139,902	
Computers	45,575	9,321	
Travel	-	-	
<b>DIRECT TOTALS</b>	<b>6,382,682</b>	<b>1,130,244</b>	<b>17.71%</b>
Indirect Costs- 10%	638,268	113,024	
<b>BUDGET TOTALS</b>	<b>7,020,950</b>	<b>1,243,268</b>	<b>17.71%</b>

**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.).”**

In response to questions raised at the February 15, 2023 stakeholders’ meeting we provide the following information:

**WSU’s Granting Policies for Charging Personnel Effort**

Each employee at Wayne State University is given a salary based on title, years of service, union guidelines, and other factors relating to that employee’s position. Salaries are paid out regardless of the number of grants a faculty member may have. Salaries support the main mission of the school of medicine, which covers research, teaching, service, and administrative activities.

When a faculty member is awarded a research grant, a portion of their salary is charged directly to the grant. The amount of salary charged to the grant is defined as effort. The federal government requires university employees charged to grants to certify their efforts on grants bi-annually. The certification process ensures that the state and federal grants are billed for an employee’s work which is reasonable in relation to the work that the employee actually performs.

When a grant application is submitted, the Principal Investigator (PI) budgets a reasonable percent of his/her effort on that project, along with other personnel efforts such as co-PIs, co-investigators, and other research support. The budget for the grant application is the PI’s best guess on how much effort will be needed for the duration of the grant, with the expectation that

the budgeted effort for the PIs/Co-PIs is the average effort for the duration of the grant. It's typical for PIs/Co-PIs to spend more time than budgeted in the first year of the grant with all the preparation work to get the study up and running. It is customary for PIs to have 30-50% of their effort charged to grants.

Efforts will fluctuate during the grant period. What was budgeted is not necessarily what will be actually charged to the grant. WSU's policy is that we charge the PI/Co-PIs effort at the budgeted amount and if they are going to reduce that effort, written approval from the granting agency is required. Efforts are monitored on a quarterly basis and as needed with personnel changes.

In many cases, a PI will have multiple grants. This does not impact their overall salary. Rather their effort will be charged to all the projects they are working in, depending on the amount of time they work on each project.

Faculty and research staff are considered direct costs to a study as these individuals work directly on projects. This is common practice at all universities. These are not considered administrative/overhead expenses. Indirect costs are budgeted and charged to grants to cover overhead expenses. The indirect cost rate for many state grants at WSU is 26% while the rate for NIH grants is 54%. The indirect cost rate for the LARA studies is 10%. In addition to the 10% rate, there were budgeted efforts (15% and lower) for the department's administrative director, grant/contract administrator, HR program specialist, and research assistant in charge of managing IRB. Again, these budgeted amounts are not necessarily what is charged to the grant. Only the administrator's effort has been charged during this progress report period.

The financial management of each grant is overseen by our Sponsored Program Administration (SPA) department at WSU. They are the oversight on each grant, ensuring efforts and all other costs are allowable based on each grant contract. They review all charges and submit the financial reports to the grant agencies.

Respectfully submitted,



Leslie H. Lundahl, PhD  
Lead/Contact Principal Investigator



David M. Ledgerwood, PhD  
Co-Principal Investigator

April 14, 2023



Sponsored Program Administration  
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### FINANCIAL STATEMENT

Agency State of Michigan Dept of Licensing & Regulatory Affairs	WSU Index No. 370718M & 380156SUB	Report Period 01/01/23 Thru 03/31/23	Date 04/14/23	
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	Grant/Contract No. VMR202101	
CATEGORY	EXPENDITURES		AGREEMENT	
	Current Period	Cumulative	Budget	Balance
Salaries & Wages	\$94,287.37	\$706,826.72	\$3,080,771.00	\$2,373,944.28
Fringe Benefits	\$24,698.93	\$194,694.50	\$844,452.00	\$649,757.50
Travel	\$0.00	\$0.00	\$0.00	\$0.00
Supplies & Materials	\$1,651.50	\$37,849.41	\$2,328,055.00	\$2,290,205.59
General Expenses	\$0.00	\$0.00	\$0.00	\$0.00
Equipment	\$67,251.44	\$79,649.88	\$129,404.00	\$49,754.12
Tuition	\$0.00	\$0.00	\$0.00	\$0.00
TOTAL DIRECT	\$187,889.24	\$1,019,020.51	\$6,382,682.00	\$5,363,661.49
Indirect Costs Rate: 10.00%	\$18,788.92	101,902.05	\$638,268.00	\$536,365.95
TOTAL EXPENDITURES	\$206,678.16	\$1,120,922.56	\$7,020,950.00	\$5,900,027.44
STATUS OF REVENUE		OUTSTANDING INVOICES		
Previously Reported	\$914,244.40	Date	Invoice No.	Amount
Current Billing	\$206,678.16			
Total Expenditures	\$1,120,922.56			
Total Payments to Date	\$3,510,475.00			
Outstanding Amount	(\$2,389,552.44)			
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 Erno, Senior Director of Sponsored Program Administration	DATE: 4/14/23			

4/14/2023