People Science, Inc.

Pilot Observational Research Study Protocol

A Direct-to-Consumer, randomized, double-blind, placebo-controlled, double cross-over study investigating the effect of specific cannabinoid products on motivation, energy level, focus, and appetite in healthy adults

Version Date: **28 June 2023**

Protocol Version: 01
Protocol Number: PS04

Sponsor: Phylos Bioscience Inc.
2455 NW Nicolai St. STE B-O6
Portland, OR 97210

Principal Investigator: Noah Craft, M.D., Ph.D.
People Science, Inc.
8605 Santa Monica Blvd,
Suite 85089
West Hollywood, CA 90069
213-328-0919
noah@peoplescience.health

Participating Sites: People Science, Single Site Study

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Abbreviation	Meaning
AE	Adverse Event
App	Application
CFR	Code of Federal Regulations
Chloe	Consumer Health Learning and Organizing Ecosystem
DTC	Direct to Consumer
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council for Harmonisation
IRB	Institutional Review Board
MEFA	Motivation, Energy Level, Focus, and Appetite Questionnaire
NIH	National Institutes of Health
PI	Principal Investigator
THC	Tetrahydrocannabinol
THCV	Tetrahydrocannabivarin
VAS	Visual Analogue Scale

1.0 OBJECTIVES AND ENDPOINTS

Objectives	Endpoints/ Measurements
Primary Objective	
To observe the effect of various cannabinoid-containing products on motivation.	Change in average motivation score by 1 point as measured by a 10-point visual analogue rating scale (VAS) collected between the cannabinoid products and placebo use sessions.
Secondary Objective	
To observe the effect of cannabinoid products on energy level, focus, and appetite.	Change in average score by 1 point as measured by a 10-point visual analogue rating scale (VAS) between the cannabinoid products and placebo use sessions.
Exploratory Objective	
To observe changes in overall symptoms and quality of life. To identify improvements for future participant centered study designs using participant feedback.	Changes in overall symptoms and quality of life to be assessed based on MEFA questionnaire responses. Evaluation of study participant experiences based on the experience survey. This may include design and use of app-based data collection tools.

2.0 INTRODUCTION: BACKGROUND INFORMATION & SCIENTIFIC RATIONALE

2.1 Introduction/Rationale for Development

Tetrahydrocannabivarin (THCV) is a rare cannabinoid and is a homologue of THC that differs only in the length of the alkyl side chain (3C vs 5C, respectively). Pre-clinical and clinical trials have shown that THCV has medical potential as a neuroprotectant, anti-inflammatory, anti-anxiety, and most notably as a therapeutic to improve glycemic control in type 2 diabetic patients.

Several THCV products are available in states with recreational cannabis. Anecdotal reports from adult cannabis users indicate that THCV provides an energizing, focusing and euphoric high–while still creating a lucid, uplifting experience. Additionally, unlike THC-dominant products, THCV was not reported to increase appetite. Other anecdotal comments referring to increased ability to focus for long periods of time and being more active were common.

Given anecdotal evidence, which shows that THCV is activating and improving focus, this provides rationale and justification to conduct a clinical research study to further test and

understand whether THCV improves motivation, focus, level of energy, and does not stimulate appetite in healthy adults.

2.2 Overview of and Rationale for the Study Design

The rationale for this study is to determine the effect of a consumer-grade, state-legal formulation of cannabinoids including Tetrahydrocannabivarin (THCV) on motivation, energy level, focus, and appetite. A consumer-driven, decentralized observational clinical research study is therefore well suited to examine the effect of this formulation in healthy individuals.

We will examine the outcomes in a broad age-range of adults who have chosen to try these products. The study will incorporate participant reported outcomes and surveys collected after each product use session to engage the participant in their typical day-to-day activities. There is no “physician-patient” relationship as part of this research since the participant as a consumer is making the informed choice to take the products and take part in the observational process with self-reported measures. Findings from this study will contribute knowledge toward the design of future cannabis research studies and the improvement of the product formulation.

A new study questionnaire was developed as no existing questionnaire would be able to capture all interest areas of this study in a holistic manner. Other questionnaires related to focus, attention, concentration, fatigue, work, and motivation were assessed and used to support the study questionnaire development.

3.0 SAMPLE SIZE, COHORT CHARACTERISTICS, ELIGIBILITY AND INVOLVEMENT

3.1 Sample Size and Cohort Characteristics

The sample size for this study will be approximately 58 healthy volunteers who meet the eligibility criteria.

3.2 Eligibility

Participants must meet all of the following criteria on screening to be considered eligible to participate in the study:

Inclusion Criteria

1. Healthy adults age ≥ 21 years old
2. Work / study / play in an environment that requires focus
3. Able to read and understand English
4. Able to read, understand, and provide informed consent
5. Able to use a personal smartphone device and download Chloe by People Science
6. Able to complete study assessments over the course of up to 14 days
7. Familiar with the use of cannabis and its effects
8. Able to tolerate at least 5mg THC
9. Willingness to abstain from use of any THC containing products during study product use days
10. Willingness to abstain from use of alcohol during study product use days

11. Greater Los Angeles area residents only

Exclusion Criteria

1. Participants who do not have a smartphone and/or internet access
2. Any known adverse effects from taking cannabis
3. Concomitant Therapies: Currently taking medication for ADHD or psychotropic medications
4. Other Illnesses or Conditions: Participants who have the following co-morbidities are excluded:
    a. History or currently undergoing product use for substance abuse disorders
    b. Currently pregnant, planning to become pregnant within the next month, or breastfeeding
    c. Allergies to formulation ingredients
    d. Current or prior psychotic disorder
    e. Immunosuppressive product uses, including organ transplant participants, active immunotherapy for cancer product use
    f. Any condition that is considered by investigator to be a contraindication to cannabis (e.g. specific drug-use interaction, unstable cardiac arrhythmia)

3.3 Duration of Participation and Overview of What is Expected from Participants

Participants will complete up to a seven week study consisting of screening period, baseline period, up to a 21-day product use period with a total of 9 product use sessions. Screening assessments, baseline questions, product use period questionnaires, adverse event reporting, and end of study experience survey data will be collected. This study will be conducted remotely and will use a web-based data collection platform, Consumer Health Learning and Organizing Ecosystem (Chloe), by People Science where participants will complete study assessments using the Chloe app during the course of the study. Participants will receive the study product during the baseline period. Demographic and medical history data will be collected for the study.

3.4 Participant Recruitment

Participants will be recruited through the People Science community, People Science website, email outreach and social media channels, in addition to Phylos' community network. Local dispensaries may also be used for recruitment purposes, as deemed appropriate by Phylos and People Science. Advertisements will be in digital format and will link to a study landing page to enable sign up.

Interested individuals will have already made the decision to try these cannabinoid products.

4.0 STUDY ACTIVITY CALENDAR

Table 4.1 Study Calendar

Protocol Activities	Screening[a]	Baseline[b]	Study Duration								
			Product Use Period 1[c] (Up to 7 Days)			Product Use Period 2[c] (Up to 7 Days)			Product Use Period 3[c] (Up to 7 Days)		
	Up to Day -14	Up to Day 14	Product Use Session 1	Product Use Session 2	Product Use Session 3 / Cross-Over	Product Use Session1	Product Use Session 2	Product Use Session 3 / Cross-Over	Product Use Session1	Product Use Session 2	Product Use Session 3 / End of Study[i]
Informed Consent	X										
Medical History	X										
Demographics	X										
Concomitant Medications	X										
Eligibility Confirmation	X										
Product Delivery Receipt		X									
Randomization[d] (Study Product, THC Only Product, or Placebo Group)		X									
MEFA Questionnaire[e]		X			X			X			X
Daily Product Use Survey[f]			X	X	X	X	X	X	X	X	X
Adverse Event Survey[g]			X	X	X	X	X	X	X	X	X
Cross-Over[h] (Study Product, THC Only, or Placebo Group)					X			X			
Experience Survey											X

a. Screening activities to occur within 14 days prior to Baseline (Day -14).

b. Baseline activities to occur up to 14 days prior to study product use sessions (Day 14).

c. Study duration to take place up to 21 days total across 7 days maximum within 3 periods.

d. Participants to be randomized into the Study Product, THC-Only Product, and Placebo groups for each Product Use Period.

e. MEFA (Motivation, Energy Level, Focus, and Appetite) Questionnaire to be administered during Baseline and at the end of Product Use 3 sessions.

f. Daily Product Use Surveys to be administered at the end of each product use session.g. Any adverse event occurrence to be reported after the product use session.

h. Participants cross-over into either Study Product, THC-Only Product, or Placebo group upon completion of Product Use Period 1 and 2.

i. Participants to complete an experience survey at the end of the study.

5.0 RECRUITMENT, CONSENT AND ENROLLMENT

5.1 Recruitment

Participants will be recruited through the People Science community, social media channels, including Facebook, Reddit, Instagram, and Google. In addition, People Science will leverage Phylos' community network for recruitment purposes, as deemed appropriate.

Recruitment outreach will consist of IRB approved advertising by email, digital flyers/postcards, and digital marketing channels (email and social media).

The IRB approved study landing page on the People Science website will lead to an IRB approved pre-screening questionnaire to determine individual qualification then collect participant first and last name, email, phone number, and zip code of qualified individuals. New leads will receive further instructions by email to determine qualification and continue through the enrollment process.

5.2 Consent

Virtual electronic informed consent, including a study specific privacy authorization and the California Experimental Subject's Bill of Rights will be provided to participants through a HIPAA compliant cloud-based platform to obtain electronic consent that will ensure that the consenting process follows all required elements (see Section 7.0). A digital copy of the signed consent will be stored with the participant's profile in the study data platform which is the same technology used for electronic consent.

5.3 Enrollment

Eligible participants who provide virtual electronic consent will be automatically registered into the study by the data platform (see Section 12.6).

6.0 STUDY PROCEDURES

6.1 Study Overview

Upon initial qualification, the participant will receive an email with study onboarding information including instructions to complete study assessments, as required. These study assessments can be accessed via the Chloe mobile app available on Apple iOS and Android devices. The participant's activities are as follows:

Screening Day -14 to Day 0:

- Complete the Informed Consent
- Complete Demographics, Medical History and Concomitant medications, including current cannabis use information (frequency, route, any previous adverse reactions from taking cannabis and tolerance in taking at least 5mg THC previously)
- Eligibility Confirmation and Enrollment

Baseline Day 1 to Day 14:

- Provide preferred delivery address for product delivery during Baseline
- Random assignment to either Study Product, THC-Only Product, or Placebo Group
- MEFA Questionnaire
- Receipt of study products within 2 weeks of eligibility confirmation
    - Participants will be asked daily if they have received their study product delivery
    - Once they confirm receipt, they will be advised on the product use period start date

Product Use Period (Up to 21 days):

- *The Participant will be randomized into either Study Product, THC-Only Product, or Placebo Group upon enrollment*

- *The Participant will be crossed-over twice into the Study Product, THC-Only Product, or Placebo Group once they have completed 3 product use sessions during the first and second product use periods*
- *The Participant will complete a total of 9 product use sessions between Study Product, THC-Only Product, and Placebo groups across a maximum of 21 days*
  - *The Study Product will contain 10mg THCV + 5mg THC in the form of a single gummy.*
- *If the participant cannot tolerate or is not comfortable with 10mg THC based on cannabis use information collected at screening, the participant may opt to cut the gummy in half and be advised to use the same dose for all product use days for the duration of the study.*

Period 1: Up to 7 days

- After 3 product use sessions:
  - Daily survey questions regarding motivation, level of energy, focus and appetite
- At the end of Period 1:
  - MEFA Questionnaire and Adverse Event Reporting

Crossover:

- Upon completion of Period 1, participants will cross-over to either the Study Product, THC-Only Product, or Placebo group for up to 7 days.

Period 2: Up to 7 days

- After 3 product use sessions:
  - Daily survey questions regarding motivation, level of energy, focus and appetite
- At the end of the Period 2:
  - MEFA Questionnaire and Adverse Event Reporting

Crossover:

- Upon completion of Period 2, participants will cross-over to either the Study Product, THC-Only Product, or Placebo group for up to 7 days.

Period 3: Up to 7 days

- After 3 product use sessions:
  - Daily survey questions regarding motivation, level of energy, focus and appetite
- At the end of the Period 2:
  - MEFA Questionnaire and Adverse Event Reporting

End of Study:

- Experience Survey
- Adverse Event Reporting

7.0 DATA COLLECTION AND MANAGEMENT

7.1 Data Collection Elements, Source, And Method Of Collection

For recruitment purposes only, a data set limited to name, email, telephone number, and Study ID number will be generated manually. For analysis, data from the assessments will include the Study ID number and demographic factors (age, gender, race, ethnicity), medications, and supplements.

7.2 Data Management

Research Data Capture System

This project will be utilizing People Science's proprietary platform, Chloe. All data is securely stored on People Science Amazon Web Services HIPAA compliant servers. The platform contains modules for building and managing forms / surveys, landing pages, marketing outreach with tracking tools for recruitment, audited electronic consent forms, data management and analytics using an integrated relational database. Data from completed assessments will automatically be collected for analysis. Study monitoring can be done using reporting features.

7.3 Data Management at Study Completion

For longer term storage of the data that will reduce risk of a data breach while still permitting that the data be verifiable (audited) the dataset will be de-identified - no names, etc., and all dates turned into time- and coded, and the key to the code will be housed in a separate location. The data will be maintained under password protection in the database.

8.0 CODING OF DATA

The dataset for recruitment (name, telephone number and Study ID number) and the data listed in Section 7.1 for analysis will be stored on a password secured database with access only to designated study team members and the study investigator.

9.0 STATISTICAL CONSIDERATIONS.

9.1 Sample Size Estimation and Justification

We anticipate screening up to 100 individuals to achieve a final sample size of approximately 50 evaluable participants. To measure our primary outcome, a single question 10-point visual analogue rating scale (VAS) will be used to reflect motivation after consumption of the Study Product, THC-Only Product, or Placebo. . The average difference in VAS responses between these 3 groups will be measured and analyzed.

Up to 20 post-product use questions, and up to 15 daily survey questions will be collected to reflect any changes in motivation, level of energy, focus, and appetite during the study period. The average difference in responses between Study Product, THC-Only Product, and Placebo will be measured and analyzed as secondary outcomes.

9.2 Projected Study Timeline - Accrual, Data/Sample Collection, Completion

The total sample size for this observational study will be approximately 58 participants.

We anticipate enrollment to be complete in 4 months. Data analysis will be complete in 2 months, and a CSR and lay summary will be complete in another 1 month. Altogether, the study duration is estimated to be 7 months.

The final analysis will take place after approximately 50 evaluable participants have completed all final study assessments (i.e. product use sessions, questionnaires, surveys). These activities will be completed approximately seven weeks after enrollees initiate participation in the study.

9.3 Evaluable Participants

Participants will be considered evaluable for analysis if they complete all assessments in at least two product use sessions within each group of the study.

9.4 Covariates and Subgroups

Demographic and baseline values will be collected and analyzed on all participants. Data on age, sex, race/ethnicity, medical history including prior cannabis use, medical diagnoses, prescriptions, alcohol use, smartphone operating system (Android or iOS) will all be collected and included in univariate, bivariate, and multivariate analyses. Subgroup analyses will be

conducted to examine differences in outcome by all covariates available.

9.5 Missing Data

Missing data will be imputed with a value of “999”. The proportion of missingness will be evaluated among all covariates and outcome variables. If data are missing on a variable in under 5% of cases and the assumption of missing completely at random can reasonably be made, only observed data will be used in the analysis. If a variable is missing within a range of 5%-40% of cases, use of multiple imputation will be evaluated. Regression analyses will be conducted using only complete cases.

9.6 Statistical Analysis Plan

The primary objective of this study is to determine the impact of Phylos’ study product on motivation as measured by the change in VAS scores from approximately 50 participants. Univariate statistics will be generated to describe the distribution of patient characteristics and outcome data. Continuous variables will be described using means, standard deviations, minimums and maximums while categorical variables will be described using counts and percentages. VAS scores will be compared from baseline pre-product use; and at end of study (post-product use) of the same individuals. We will analyze up to 58 participants to achieve at least 90% power to detect a mean change in VAS scores of 1 point (SD=2) from baseline with a type I error of 0.05 (two-sided) assuming a paired means dependent Wilcoxon Signed-Rank test. We are testing the null hypothesis that there is no difference between pre-product use and post-product use mean VAS scores within study participants. Summary statistics will be generated, and paired differences between pre-product use and post-product use VAS scores will be reported, along with 95% confidence intervals.

Additionally, parametric linear mixed models will be employed to simultaneously account for correlated observations and adjust for confounding variables (Proc Mixed, SAS). Several covariance structures, including compound symmetry and unstructured, will be evaluated by comparing AIC and BIC to identify optimal model fit. Random slope and intercept will also be considered in a similar manner. Patient characteristics (i.e. age and sex) will be included in adjusted models a priori for confounding control. Directed acyclic graphs will be employed to select other potential confounding variables and identify biases during the model fitting process. Large differences will be further examined and may help identify where further calibration of estimation models are needed.

Stratified and interaction analyses will be employed to detect between-subgroup differences in outcomes. Specifically, we will test the difference in VAS score change between Study Product, THC-Only Product, and Placebo groups. Testing of these differences will be conducted by including 2-way product terms between the exposure and covariate of interest in linear mixed modeling. A significant interaction will be defined by an interaction coefficient with a p-value < 0.05.

9.7 Reporting Conventions

Confidence intervals and p-values will be reported at two decimal places, except when p-values are less than 0.01. P-values less than 0.01 will be reported as “< 0.01” and p-values less than 0.001 will be reported as “<0.001”.

9.8 Quality Assurance of Statistical Programing

SAS 9.4 will be used for all data analyses in a Microsoft Windows environment. All analysis code will include the author’s name, date/time of writing, reference to location and nature of inputs, reference to any parent code, and detailed comments to aid in its interpretation and implementation. A secondary statistician will have access to raw data and the opportunity to

independently create the main analyses. They will also be given access to the primary code to review its validity.

10.0 STUDY COMPLIANCE AND REPORTING OF DEVIATIONS FROM APPROVED PROCEDURES

Deviations

A deviation is a divergence from a specific element of a protocol and that occurred without prior IRB approval. Deviations from the approved protocol should be avoided, except when necessary to eliminate an immediate hazard to a research participant. All deviations from the protocol will be documented in study source documents and promptly reported to the IRB.

Reporting Deviations

Investigators may deviate from the protocol to eliminate immediate hazards for the protection, safety, and well-being of the study subjects without prior IRB approval. For any such deviation, the PI will notify the IRB, within 5 calendar days of its occurrence by electronic submission of a deviation notice.

11.0 STUDY OVERSIGHT, QUALITY ASSURANCE, AND DATA & SAFETY MONITORING

The study team will be familiar with anticipated and unanticipated adverse experiences. The Principal Investigator (PI) is responsible for monitoring protocol conduct and reporting to the Institutional Review Board (IRB).

12.0 ETHICAL AND REGULATORY CONSIDERATIONS

12.1 Ethical and Regulatory Standard

Ethical Standard

This study will be conducted in conformance with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979) and the Declaration of Helsinki.

Regulatory Standard

This study is to be conducted in compliance with the IRB approved protocol and according to applicable federal, state, local and tribal laws including the following:

- US Code of Federal Regulations (CFR) governing clinical study conduct: Title 45 Part 46 – Protection of Human Subjects
- US Code of Federal Regulations relating to the Health Insurance Portability and Accountability Act of 1996: Title 45 Part 164 – Security and Privacy – Subpart E - ○ Subpart E—Privacy of Individually Identifiable Health Information
- State of California Health and Safety Code, Title 17, for research conducted in California

In addition, this study is to be conducted in compliance with applicable policies and procedures of the IRB(s) of record, applicable institutional research policies and procedures, applicable institutional clinical policies and procedures, and applicable NIH policies and procedures.

Institutional Review Board

The protocol, informed consent form(s), recruitment materials and all participant materials will be submitted to the IRB of record for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendments to the protocol or consent materials will require review and approval by the IRB before the changes

are implemented in the study.

Per the federal regulations at 45 CFR 46 and State of California Health and Safety code, Title 17, must review and approve this protocol and the informed consent process and its documents prior to initiation of the study. All institutional, NIH, Federal, and State of California regulations must be fulfilled.

Any documents that the IRB may need to fulfill its responsibilities (such as protocol, protocol amendments, consent forms, information concerning participant recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB. The IRB's written unconditional approval of the study protocol and the informed consent document will be in the possession of the investigator before the study is initiated.

Any amendment to the protocol document and accompanying informed consent documents, as developed and provided by the PI, will require review and approval by the IRB of record before the changes are implemented in the study.

12.2 Risk Benefit Considerations

Discomforts, Risks, and Risk Mitigation

- Risks associated with the Survey: The questions used in this survey may cause temporary discomfort or distress to the participant. The survey is designed to be simple and short and is a commonly used tool in clinical studies. The participant may choose not to complete the questionnaire.
- Risks associated with Breach of Confidentiality: There is minimal risk that people who are not connected with this study will learn of the participant's identity or personal information. The study staff will be GCP trained and will utilize best practices when using the data platform to ensure participant privacy protections.

Risk Level Determination

The risks to the study are minimal or unanticipated due to appropriate mitigation measures (e.g. breach of confidentiality, loss of internet access). This research meets the federally defined definition of minimal risk (45CFR 46.102(j)).

Direct benefit to research participants

Research participants have the opportunity to engage with scientists in tracking the effect THCV may have on their motivation, energy level, focus, and appetite. Participants will receive $50 upon completion of study activities.

Importance of the knowledge that may reasonably be expected

This research is significant and important because increasing knowledge and experience in using a personal device with the ability to connect with health providers virtually may ultimately change the delivery of healthcare.

12.3 Participant Characteristics

Research equity

This research has no direct exclusions related to gender. There are also no direct exclusions related to race or ethnicity.

Vulnerable Populations

Pregnancy and lactation are exclusions due to the unknown risks of cannabis product use to fetuses and newborns.

Volunteers with impaired decision-making capacity are excluded.

Volunteers unable to personally provide informed consent (including but not exclusive of inability to speak and read English, hearing or sight impaired, etc.) will be excluded from participating in this research.

12.4 Financial Obligation, Burden, and Compensation to Participants

Completing research activities (not from results/findings or injury)

Research activities will be conducted virtually.

Participants will receive compensation for their time. A $50 gift card will be provided by study staff to participants upon study completion.

Research results or clinical findings arising from research activities

Due to the nature of the study, it is unlikely that research results or findings from research activities will result in further medical-related expenses for the participant.

12.5 Confidentiality/Sharing/Publication

Return or Clinical Use of Research Results

Participants will be shown their study data in real time as they go through the data visualization modules in the Chloe platform.

Research results will be shared with participants at completion of data analysis. The results of this research may help the participant make decisions in future product purchases and participate in future research studies.

There are no anticipated burdens or financial obligations to research subjects.

Confidentiality

All documents and electronic data will be stored on secure, password-protected computers or cloud-based servers. Participant confidentiality will be strictly held in trust by the investigators, study personnel, and sponsor. No identifiers will be used in any subsequent publication of these results.

Information/Data Retention, Future Use, and Sharing

All personal information provided by participants is the property of such participants and a copy of such information will be shared with People Science. The Study Sponsor will have access to de-identified data. Participants have the right to request that their account and associated personal information be deleted. A participant's information will remain with People Science as long as the participant is active in the study and/or has an active account and has not requested that his or her account be deactivated and his/her information be deleted.

Publication

The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996. Neither the complete nor any part of the results of the study carried out under this protocol, nor

any of the information provided by the sponsor for the purposes of performing the study, will be published or passed on to any third party without the written approval of the Study PI. Any investigator involved with this study is obligated to provide the sponsor with all data derived from the study.

12.6 Alternatives to Participation, Withdrawal, and Early Termination

Alternatives to Participation

The individual can choose not to participate.

Participant Withdrawal from Research/ Research Activities

Research activities are limited to approximately seven weeks.

Participants may withdraw from the study at any time and for any reason without prejudice. The withdrawal must be documented.

12.7 Informed Consent, HIPAA Authorization, and California Subject's Bill of Rights

Informed Consent

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Operational details specific to the consenting process that occurs prior to any research evaluations/interventions are described in Section 6.0.

All participants will undergo virtual electronic informed consent after they are determined to qualify for the study. An electronic informed consent document will describe the nature, duration, purpose of the study, potential risks, alternatives and potential benefits, and all other IRB approved information. In addition, the experimental participant's bill of rights and the HIPAA research authorization form will be provided. Prospective research participants will be informed that they may withdraw from the study at any time and for any reason without prejudice. Prospective research participants will be afforded sufficient time to consider whether to participate in the research.

Virtual informed consent will be conducted through the app-based consent form at the participant's convenience. After reading the consent, participants will be able to contact study staff about any study related questions. Once the prospective participant expresses full understanding, virtual informed consent will be obtained through electronic signature from either the prospective participant before study participation. The method of obtaining and documenting the informed consent and the contents of the consent must comply with the ICH-GCP and all applicable regulatory requirements. A copy of the signed consent document will be available to the participant within the Chloe app. The signed consent must be maintained by the investigator and available for inspection by sponsor designated representatives, or regulatory authority at any time.

Privacy Authorization

The informed consent process will include a privacy authorization compliant with 45CFR164.508(c) via the inclusion/incorporation of:

- all core elements specified in 508(c)(1) including the signature of the individual (or representative) and date of signature,
- all required statements specified in 508(c)(2)

- the plain language requirement as specified in 508(c)(3), and
- the provision to the participant (or representative) a copy of the signed authorization (508(c)(4)

State of California Human Experimentation Requirements

This research involves the collection of information via validated questionnaires and obtaining information from the medical record. Research activities do not encompass those that are requisite for a participant to be involved in a “medical experiment” as defined by California State Law 24174. The ‘California Experimental Subject’s Bill of Rights’ will be administered as part of the informed consent process; as part of that process participants will receive a copy of the ‘Bill of Rights’ marked with their signature.

12.8 Investigator Conflict of Interest

Investigators will disclose any conflict of interest from People Science.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study Sponsor prior to participation in this study. All investigators will follow the conflict of interest policy.

13.0 REFERENCES

1. *García C, Palomo-Garo C, García-Arencibia M, Ramos J, Pertwee R, Fernández-Ruiz J. Symptom-relieving and neuroprotective effects of the phytocannabinoid-THCV in animal models of Parkinson's disease. Br J Pharmacol. 2011 Aug;163(7):1495-506. doi: 10.1111/j.1476-5381.2011.01278.x. PMID: 21323909; PMCID: PMC3165958.*

2. *Bolognini, D., Costa, B., Maione, S., Comelli, F., Marini, P., Di Marzo, V., Parolaro, D., Ross, R.A., Gauson, L.A.,Cascio, M.G. and Pertwee, R.G. (2010), The plant cannabinoid-tetrahydrocannabivarin can decrease signs of inflammation and inflammatory pain in mice. British Journal of Pharmacology, 160: 677-687. https://doi.org/10.1111/j.1476-5381.2010.00756.x*

3. *Cascio MG, Zamberletti E, Marini P, Parolaro D, Pertwee RG. The phytocannabinoid ^{9}-tetrahydrocannabivarin, can act through 5-HT$_{1}$A receptors to produce antipsychotic effects. Br J Pharmacol. 2015 Mar;172(5):1305-18. doi: 10.1111/bph.13000. PMID: 25363799; PMCID: PMC4337703.*

4. *Wargent ET, Zaibi MS, Silvestri C, Hislop DC, Stocker CJ, Stott CG, Guy GW, Duncan M, Di Marzo V, Cawthorne MA. The cannabinoid Δ(9)-tetrahydrocannabivarin (THCV) ameliorates insulin sensitivity in two mouse models of obesity. Nutr Diabetes. 2013 May 27;3(5):e68. doi: 10.1038/nutd.2013.9. PMID: 23712280; PMCID: PMC3671751.*

5. *Jadoon KA, Ratcliffe SH, Barrett DA, Thomas EL, Stott C, Bell JD, O'Sullivan SE, Tan GD. Efficacy and Safety of Cannabidiol and Tetrahydrocannabivarin on Glycemic and Lipid Parameters in Patients With Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Pilot Study. Diabetes Care. 2016 Oct;39(10):1777-86. doi: 10.2337/dc16-0650. Epub 2016 Aug 29. PMID: 27573936.*