CLINICAL STUDY REPORT

CLIP Study

Pharmacokinetic study of a novel lipid formulation of cannabidiol (CBD)

Sponsor Protocol Code:	CLIP Study
EudraCT Number:	2020-004551-33
ClinicalTrials.gov Identifier:	NCT05032807
ISRCTN number:	18067579
REC Number:	22/LO/0047
Investigational Drugs (IMPs):	Cannabidiol (CBD): novel lipid formulation (SEEK-CBD) and standard powder formulation (STD-CBD)
Indication:	Pharmacokinetic evaluation of oral cannabidiol formulation in healthy volunteers
Development Phase:	Phase 1 CTIMP pharmacokinetic study
Study Begin (FPFV):	15 June 2022
Study End (LPLV):	09 September 2022
Report Version & Issue Date:	Version 1.0, 18 May 2026
Co-sponsor Name and Address:	King's College London, King's Health Partners Clinical Trials Office, F16, Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT
Co-sponsor contact details:	Krista Wills; +44 (0)20 7188 5732; krista.wills@kcl.ac.uk
Chief Investigator:	Professor Philip McGuire, Institute of Psychiatry, Psychology and Neuroscience, De Crespigny Park, London SE5 8AF

SIGNATURE PAGE

By signing below I approve the contents of this Clinical Study Report, and confirm that to the best of my knowledge it accurately describes the conduct and results of the study. The clinical trial reported herein was conducted in accordance with the principles contained in the Declaration of Helsinki, Good Clinical Practice (GCP) and all applicable laws and regulations.

This was a non-commercial academic trial, the results of this study are not intended to be used or a licensing application.

Chief Investigator: Allan Young

Printed name	**Signature**	**Date**

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1. Ethics

Independent Ethics Committee or Institutional Review Board

The study protocol and amendments were reviewed by London - Brent Research Ethics Committee. The REC reviewed the application at its meeting on 24 January 2022 and issued a favourable ethical opinion with conditions on 31 January 2022 (REC reference 22/LO/0047; IRAS project ID 288415; EudraCT 2020-004551-33).

Ethical conduct of the study

The trial was conducted according to the approved protocol and in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice (GCP), the Medicines for Human Use (Clinical Trials) Regulations 2004 as amended, the UK Policy Framework for Health and Social Care Research, data protection requirements and other applicable regulatory requirements. The clinical trial authorisation process included review by the MHRA.

Subject information and consent

Participants were healthy volunteers recruited through approved advertisements. Potential participants contacted the research team by email, received the participant information sheet, completed pre-screening by telephone and attended a screening visit at the NIHR-Wellcome Trust King's Clinical Research Facility. Written informed consent was obtained before trial-specific procedures. The study enrolled healthy volunteers rather than patients.

2. Data Monitoring

No independent Data Monitoring Committee or Trial Steering Committee was convened. The protocol specified that, because this was a small, short-duration pharmacokinetic study with minimal expected risk based on published cannabidiol safety data, formal committees were not required. Safety and pharmacovigilance oversight were retained by the Chief Investigator and King's Health Partners Clinical Trials Office on behalf of the Sponsor.

3. Sponsors, Chief Investigator and Trial Sites

Sponsors or Co-Sponsors	King's College London King's Health Partners Clinical Trials Office F16, Tower Wing, Guy's Hospital Great Maze Pond London SE1 9RT

Chief Investigator	Professor Philip McGuire Institute of Psychiatry, Psychology and Neuroscience De Crespigny Park London SE5 8AF Professor Allan Young Institute of Psychiatry, Psychology and Neuroscience De Crespigny Park London SE5 8AF
Trial Sites	NIHR King's Clinical Research Facility London, United Kingdom

4. Co-Investigator(s), Statistician, Laboratories, Database Management

Co-Investigator(s)	Dr Edward Chesney, Co-investigator, King's College London Professor Mitul Mehta, Co-investigator, C-FIT, King's College London Eric Lynch, Co-investigator, C-FIT, King's College London Ndabezinhle Mazibuko, Co-investigator, C-FIT, King's College London
Statistician	Oranuch Nampaisan, Statistician, Grand Pacific CRO
Laboratories	Turku Metabolomics Centre, University of Turku and Abo Akademi University, bioanalysis Oxford Centre for Microbiome Studies, stool sample storage/analysis
Database Management	*King's Clinical Trials Unit*

5. Study Synopsis

Title of clinical trial	Pharmacokinetic study of a novel lipid formulation of cannabidiol (CBD)
Protocol Short Title/Acronym	CLIP Study / CBD-Lipid-PK
Study Phase	Phase 1 CTIMP pharmacokinetic study
Sponsor name	King's College London
Chief Investigator	Professor Philip McGuire
EudraCT number	2020-004551-33
REC number	22/LO/0047
IRAS project ID:	288415
Medical condition or disease under investigation	Healthy volunteers; pharmacokinetics and bioavailability of oral cannabidiol
Purpose of clinical trial	To compare systemic exposure to CBD after a single 1000 mg oral dose administered as a novel lipid formulation versus a standard CBD-only powder formulation in the fasting state.
Primary objective	To assess whether the novel lipid formulation increases the bioavailability of oral CBD in the fasting state.
Secondary objective (s)	To characterise and compare the pharmacokinetic profiles of the novel CBD formulation and the standard formulation; exploratory assessment of associations between gut microbiome features, bile acids, endocannabinoids and CBD metabolism.
Trial Design (e.g. randomised, double-blind, treatment arms, and duration of study)	Single-centre, double-blind, two-period crossover pharmacokinetic study in healthy volunteers.
Endpoints	Primary: AUCinf for CBD. Secondary: Cmax, Tmax, AUC0-48 and t1/2. Safety: treatment-emergent AEs, vital signs, laboratory tests, urinalysis and GSRS.
Planned number of subjects	14 healthy volunteers
Study population (inclusion/exclusion)	Healthy volunteers aged 18-45 years, healthy on clinical history, physical examination, ECG, vital signs, blood and urine tests; able to provide written informed consent and fast on dosing days. Key exclusions included relevant medical history, prescribed medication other than contraception, recent CBD/OTC/supplement use, BMI <18 or >30 kg/m2, alcohol intake >14 units/week, smoking >10 cigarettes/day, illicit substance use within 6 months, pregnancy/breastfeeding, abnormal renal/liver function, positive urine drug screen or positive alcohol breath test.
Treatment per study arm (IMP, dosage and route of	Cannabidiol 1000 mg orally as five 200 mg capsules.

administration)	SEEK-CBD lipid formulation containing CBD with Gelucire 43/01, Maisine CC and PEG 400.
Results (Efficacy & Safety)	*The primary endpoint was met. CBD exposure was substantially greater after SEEK-CBD than after STD-CBD.* *Geometric mean AUCinf was 674.98 h.ng/mL for SEEK-CBD and 134.76 h.ng/mL for STD-CBD (geometric mean ratio 5.0, 95% CI 2.5 to 9.9; p=0.001).* *There were no serious adverse events. Any adverse event occurred in 11/14 participants (78.6%) after SEEK-CBD and 8/14 participants (57.1%) after STD-CBD. Somnolence was reported in 7/14 participants (50.0%) after SEEK-CBD and 2/14 participants (14.3%) after STD-CBD. Gastrointestinal disorders occurred in 5/14 participants (35.7%) after SEEK-CBD and 2/14 participants (14.3%) after STD-CBD.*
Conclusions	*In fasting healthy volunteers, a single 1000 mg dose of CBD administered as the SEEK-CBD lipid formulation produced substantially greater systemic CBD exposure than the standard CBD powder formulation. T*
Version and date of protocol amendments	v1.0, 29 Nov 2021 v1.1, 10 Jan 2022 v1.2, 12 Apr 2022 v1.3, 19 May 2022
Global start of trial date / First patient first visit (FPFV)	15 June 2022
Global end of trial date / Last patient last visit (LPLV).	26 August 2022
Completion date for primary data analysis	13 January 2023

6. Glossary of terms

N/A

7. Publication (reference)

Chesney E, Mazibuko N, Oliver D, Minichino A, Lamper AD, Chester L, Reilly TJ, Lloyd M, Krakstrom M, Dickens AM, et al. Novel Lipid Formulation Increases Absorption of Oral Cannabidiol (CBD). Pharmaceutics. 2024;16:1537. https://doi.org/10.3390/pharmaceutics16121537

8. Study period (years)

The first participants provided informed consent on 15 June 2022. Trial procedures were conducted from June to August 2022 at the NIHR King's Clinical Research Facility, King's College Hospital, London. The last participant last visit date was 26 August 2022; the final follow-up occurred 7-14 days after the second dosing session.

9. Phase of development

Phase 1 CTIMP pharmacokinetic study in healthy volunteers.

10. Objectives

Primary objective: To assess whether the novel lipid formulation increases the bioavailability of oral CBD in the fasting state.

Secondary objective: To characterise and compare the pharmacokinetic profiles of the novel CBD formulation and the standard formulation.

11. Background and Context

Cannabidiol (CBD) is approved for rare childhood epilepsies and is being developed for other central nervous system disorders. Standard oral CBD has poor and variable bioavailability because CBD is highly lipophilic, is poorly absorbed in the fasting state, and undergoes extensive first-pass hepatic metabolism. Food, particularly high-fat food, substantially increases CBD exposure. The CLiP study tested whether a novel lipid matrix formulation could increase absorption in the fasting state and reduce variability related to food or gastrointestinal factors. The formulation contained Maisine CC, Gelucire 43/01 and PEG 400 and was compared with a standard CBD-only powder formulation at a 1000 mg dose.

12. Methodology

This was a single-centre, double-blind, two-period crossover pharmacokinetic study in healthy volunteers. Participants attended one screening visit, two 48-hour experimental visits separated by at least a 2-week washout, and a final follow-up 7-14 days after the second dosing session.

Table 1: Schedule of events

	Screening Visit Day -28 to day 0	Experimental visits 1 & 2*			Follow up visit
		Day 1	Day 2	Day 3	7-14 days after experiment 2 day 1
Consent	X				
Demographic information	X				
Medical Assessment**	X				
Height, weight, body fat	X				

Eligibility Review	X	X			
Urine Pregnancy test	X	X			X
Urine Drug Screen	X	X			
Alcohol breath test	X	X			
Fasting		X			
Drug Administration		X			
Intravenous Cannulation		X			
Blood sampling (FBC, LFTS, U&Es)	X	X			
Blood sampling (CBD and metabolites)		X	X	X	
Urinalysis	X	X			
Vital Signs	X	X	X	X	
Drug Effects Questionnaire (DEQ-5)		X	X	X	
Gastrointestinal Symptom Rating Scale		X	X	X	
Stool Sample Kits	X				
Adverse events		X	X	X	X
Washout period*				X	
*Minimum 2 weeks between experimental visits **Includes physical exam, vital signs, urine drug screen, alcohol breath test, blood test (U&Es, LFTs, FBC)					

Trial Medication
Cannabidiol 1000 mg oral, single dose

13. Number of participants (planned and analysed)

13.1 Planned

The study required 12 complete datasets. Allowing for approximately 15% dropout, planned recruitment was 14 participants.

13.2 Analysed

Seventeen participants were registered. Two were not randomised because they did not meet inclusion/exclusion criteria. Fifteen were randomised. Fourteen were randomised and treated, completed dosing, completed the study, and were included in the PK and safety analysis populations. One randomised

participant was not treated and was excluded from the PK and safety analysis populations for administrative reasons.

Seventeen participants were registered/screened; 15 were randomised; 14 received study drug and completed both dosing sessions. No treated participant failed to complete treatment.

Table 2: Number of patients screened, randomised, and withdrew for each arm

	N
# patients screened	17
# participants randomised/treated/study arm	15
# participants completed/study arm	14
# participants that did not complete the study	1

Table 3: The reasons for participant withdrawal from the study for each study arm

P010017	**Randomised but not treated; excluded from PK and safety populations for investigator discretion/administrative reasons.**
Treated participants	No treated participant failed to complete dosing or withdrew after study drug administration.

No treated participant withdrew after dosing. One randomised participant (P010017) was not treated and was excluded from the PK and safety populations for investigator discretion/administrative reasons.

Table 4: Planned and Actual Number of Participants Enrolled per Country

Trial country	*Planned number of participants*	*Actual number of participants enrolled*
United Kingdom	*14*	*14*

14. Diagnosis and main criteria for inclusion

The study recruited healthy volunteers aged 18-45 years. Healthy status was determined by clinical history, physical examination, ECG, vital signs and laboratory tests of blood and urine. Participants were required to be capable of giving informed consent, provide written informed consent and agree to fast on dosing days. Key exclusions included clinically relevant medical history, abnormal ECG/vital signs/laboratory values, prescribed medication other than contraception, recent CBD products, recent OTC medications or supplements, BMI <18 or >30 kg/m2, alcohol intake >14 units/week, smoking >10 cigarettes/day, illicit substance use within the previous 6 months, pregnancy/breastfeeding, abnormal renal/liver function, positive urine drug screen,

positive alcohol breath test, recent participation in another trial, hypersensitivity to CBD or formulation excipients, or inability to swallow capsules.

15. Test product, dose and mode of administration

IMP: The novel SEEK-CBD formulation contains the following excipients:

- Gelucire 43/01 (glycerides only; hard fat [EP]), manufactured by Gattefosse
- Maisine CC (glyceryl monolinoleate), manufactured by Gattefosse
- PEG 400 (polyethylene glycol 400)

All treated participants received 1000 mg CBD as SEEK-CBD and 1000 mg CBD as STD-CBD according to their randomised sequence.

16. Duration of treatment

Each participant received a single dose of CBD at each of two experimental visits. Each visit lasted 48 hours for pharmacokinetic sampling, with a minimum 2-week washout between dosing sessions and final follow-up 7-14 days after the second dosing session.

17. Reference therapy, dose and mode of administration

The active comparator/reference formulation was STD-CBD, a standard CBD-only powder formulation. It was administered orally at the same 1000 mg dose and in identical capsules.

18. Criteria for evaluation: Endpoints

18.1 Efficacy

Primary endpoint
Difference in AUCinf for a single 1000 mg oral dose of CBD between SEEK-CBD and STD-CBD in the fasting state.

Secondary Efficacy Parameters
Differences between novel and standard formulations for:

i. Maximum plasma concentration (C_{max})
ii. Time after administration of drug when maximum plasma concentration is reached (T_{max})
iii. Plasma half-life ($t_{½}$)
iv. Area under the concentration-time curve from time zero to 48hours (AUC_{0-48})

18.2 Safety

Safety Parameters
Adverse events (self-reported)
Vital signs
Full blood count, Urea and electrolytes, and Liver function tests
Urinalysis (bedside test)

Specific Safety Endpoints
Number and proportion of participants with AEs/SAEs/SARs/SUSARs; AE severity and relationship to study drug; clinically significant abnormalities in laboratory parameters, urinalysis or vital signs; gastrointestinal symptom ratings after dosing.

19. Statistical Methods

The endpoints below are based on the approved protocol and statistical analysis plan.

Analysis of Efficacy Variables
Pharmacokinetic parameters were summarised descriptively. Plasma concentration-time data were analysed using non-compartmental pharmacokinetic analysis. Log-transformed AUC and Cmax values were entered into linear mixed models to account for repeated measures and between-subject conditions. Linear contrasts for formulation differences were expressed as geometric mean ratios with 95% confidence intervals, with inference based on $p<0.05$. Wilcoxon signed-rank tests were used to compare geometric means of pharmacokinetic concentrations at each time point.

Analysis of Safety Variables
Adverse events were listed and summarised by treatment, system organ class/preferred term, severity, seriousness and relationship to study drug. Treatment-emergent adverse events were defined as any adverse event occurring after drug administration. Treatment-related events were those assessed as at least remotely related. The incidence of adverse events was compared using McNemar's test. GSRS scores were compared using Wilcoxon signed-rank tests. Vital signs at each timepoint were compared using paired t-tests.

20. Changes in the Trial Plan

No major protocol changes.

20.1 Protocol Deviations

No serious breaches or major protocol deviations

21. Summary – Conclusions

21.1 Demographic data

The following tables summarise the demographics of the study population:

Number of Participants			
Age (years)	**Male**	**Female**	**Total**
Adults (18-64 years)	7	7	14
Total	7	7	14

The participants were of white (n = 10; 71.4%) or Asian (n = 4, 28.6%) ethnicity.

21.2 Primary outcome

The primary endpoint was met. CBD exposure was substantially greater after SEEK-CBD than after STD-CBD.

Geometric mean AUCinf was 674.98 h.ng/mL for SEEK-CBD and 134.76 h.ng/mL for STD-CBD (geometric mean ratio 5.0, 95% CI 2.5 to 9.9; p=0.001).

AUC0-48 was 611.42 h.ng/mL versus 66.79 h.ng/mL (geometric mean ratio 9.2, 95% CI 5.3 to 15.7; p<0.001).

Cmax was also higher for SEEK-CBD (73.00 ng/mL versus 3.11 ng/mL; geometric mean ratio 23.4, 95% CI 11.0 to 50.0; p<0.001).

21.3 Safety results

There were 31 treatment-emergent adverse events in the safety population. Eleven participants (78.6%) experienced at least one AE after SEEK-CBD and 8 participants (57.1%) after STD-CBD.

No serious adverse events, serious adverse reactions, SUSARs or deaths were reported. Blood and urine samples collected 4 hours post-dose showed no clinically relevant abnormalities. No clinically relevant differences in vital signs were identified.

By treatment, any adverse event occurred in 11/14 participants (78.6%) after SEEK-CBD and 8/14 participants (57.1%) after STD-CBD. Somnolence was reported in 7/14 participants (50.0%) after SEEK-CBD and 2/14 participants (14.3%) after STD-CBD. Gastrointestinal disorders occurred in 5/14 participants (35.7%) after SEEK-CBD and 2/14 participants (14.3%) after STD-CBD.

Table: Listing of Adverse Events for all patients

Adverse Events	**SEEK CBD**	**Standard CBD**
Total Number of AEs per Study Arm	18	13
Participants affected by non-serious adverse events	11	8

Table: Listing of Serious Adverse Events for all participants

Serious Adverse Events	**SEEK CBD**	**Standard CBD**
Participants affected by SAEs	0	0
Total Number of SAEs per Study Arm	0	0
Total number of all cause deaths per Study Arm	0	0
Total number of deaths resulting from adverse events per Study Arm	0	0

Within the safety/PK population (n=14), a total of 31 AEs, including 0 SAEs, were identified as treatment-emergent and included in the safety analysis. Summary tables for AEs and ARs are presented in the appendix of this synopsis.

There were 0 Serious Adverse Reactions (SARs), 0 unexpected SARs and 0 SUSARs.

22. Conclusion

In fasting healthy volunteers, a single 1000 mg dose of CBD administered as the SEEK-CBD lipid formulation produced substantially greater systemic CBD exposure than the standard CBD powder formulation. The effect was evident for AUCinf, AUC0-48 and Cmax. The treatment was generally well tolerated. Somnolence was more frequently reported after the lipid formulation, but no serious adverse events, serious adverse reactions, SUSARs or deaths occurred. These results support the conclusion that the lipid formulation increases oral CBD absorption in the fasting state.

23. Date of Report

This is version 1.0 of the Clinical Study Report synopsis, dated 19 May 2026

APPENDICES

i) Summary of treatment-emergent AEs in the per protocol population

System Organ Class	Preferred Term	Number of Subjects Experiencing the AE in Active Arm	Total Number of Occurrences of the AE	Number of Subjects Experiencing the AE in Placebo Arm	Total Number of Occurrences of the AE
Gastrointestinal disorders	Abdominal distension	1 (7.1%)	1	-	-
Gastrointestinal disorders	Abdominal pain	1 (7.1%)	1	-	-
Gastrointestinal disorders	Diarrhoea	2 (14.3%)	2	-	-
Gastrointestinal disorders	Flatulence	1 (7.1%)	1	1 (7.1%)	1
Gastrointestinal disorders	Nausea	1 (7.1%)	1	1 (7.1%)	1
Gastrointestinal disorders	Vomiting	-	-	1 (7.1%)	1
Nervous system disorders	Dizziness	1 (7.1%)	1	1 (7.1%)	1
Nervous system disorders	Headache	-	-	1 (7.1%)	1
Nervous system disorders	Somnolence	6 (42.9%)	6	2 (14.3%)	2
Nervous system disorders	Tiredness	-	-	1 (7.1%)	1
Nervous system disorders	headache	2 (14.3%)	2	2 (14.3%)	2
Psychiatric disorders	Anxiety	1 (7.1%)	1	-	-
Psychiatric disorders	Feeling relaxed	-	-	1 (7.1%)	1
Psychiatric disorders	Somnolence	1 (7.1%)	1	-	-
Psychiatric disorders	high	-	-	1 (7.1%)	1
Psychiatric disorders	vasovagal episode post-cannulation	1 (7.1%)	1	-	-
Psychiatric disorders	vasovagal post-cannula	-	-	1 (7.1%)	1

ii) Summary of treatment-emergent ARs in the per protocol population

Treatment-related events were defined as events assessed as remotely, possibly, probably or definitely related to study drug.

System Organ Class	Preferred Term	SEEK-CBD subjects	SEEK-CBD occurrences	STD-CBD subjects	STD-CBD occurrences
Gastrointestinal disorders	Abdominal distension	1 (7.1%)	1	-	-
Gastrointestinal disorders	Abdominal pain	1 (7.1%)	1	-	-
Gastrointestinal disorders	Diarrhoea	2 (14.3%)	2	-	-
Gastrointestinal disorders	Flatulence	1 (7.1%)	1	1 (7.1%)	1
Gastrointestinal disorders	Nausea	1 (7.1%)	1	1 (7.1%)	1
Gastrointestinal disorders	Vomiting	-	-	1 (7.1%)	1
Nervous system disorders	Dizziness	1 (7.1%)	1	1 (7.1%)	1
Nervous system disorders	Headache	-	-	1 (7.1%)	1
Nervous system disorders	Somnolence	3 (21.4%)	3	2 (14.3%)	2
Nervous system disorders	Tiredness	-	-	1 (7.1%)	1
Nervous system disorders	headache	2 (14.3%)	2	2 (14.3%)	2
Psychiatric disorders	Feeling relaxed	-	-	1 (7.1%)	1
Psychiatric disorders	high	-	-	1 (7.1%)	1

iii) Summary of treatment-emergent SAEs in the study population

No treatment-emergent serious adverse events were reported.

iv) Summary of treatment-emergent SARs in the study population

No treatment-emergent serious adverse reactions were reported.