Australian Government
National Health and Medical Research Council

NHMRC

SAPPHIRE

Application Report

Application Details	
Grant Opportunity:	2021 Clinical Trials and Cohort Studies
Application ID:	2014980
Application Title:	A randomised controlled trial of cannabidiol (CBD) in the treatment of cannabis dependence
Chief Investigator A:	Prof Nicholas Lintzeris
Administering Institution:	University of Sydney
Grant Duration:	4 years

Contents

Participating Institutions

Participating Institutions	
Participating Institution	**Department**
University of Sydney	Department of Addiction Medicine, Faculty of Medicine and Health
South Eastern Sydney Local Health District	Drug and Alcohol Services
Sydney Local Health District	Drug Health Services and RPAH laboratory
Northern Sydney Local Health District	Mental Health and Drug and Alcohol Services
Hunter New England Local Health District	Drug and Alcohol Services
Western Sydney Local Health District	Drug and Alcohol Services
Turning Point, Eastern Health	Box Hill and Richmond campuses (2 sites)
NSW User's & AIDS Association	
Aboriginal Health and Medical Research Council of NSW	
Central Coast Local Health District	Drug and Alcohol Services
Monash University	Monash Addiction Research Centre
The University of Newcastle	School of Medicine and Public Health
University of Wollongong	School of Psychology, Faculty of Science
University of Bath	Addiction and Mental Health Group, School of Psychology

Is this application using services provided by a research facility? No
If yes, see separate attachment for details

Does this research proposal include an Aboriginal and/or Torres Strait Islander health research or capacity building component? Yes

Does your Research Proposal include a one page modified PdCCRS research proposal with reduced aims and timeframes? Not Applicable

Funding Sources

Funding Sources	
Funding is sought from the following organisation(s):	
NHMRC	Yes
Cancer Australia and Funding Partners	No

Synopsis

Synopsis

Cannabis use disorder (CUD) is increasingly common, affecting >150,000 Australians in 2019, and contributes to a range of health and social problems. Counselling, the best available treatment to-date, achieves only modest outcomes, and effective medications are needed as an adjunct to counselling. CUD is highly prevalent in Aboriginal and Torres Straight Islander communities, yet no prior study has evaluated CUD interventions in Indigenous Australians.

Promising pilot data suggests that cannabidiol (CBD, a medicinal cannabinoid with anxiolytic and antipsychotic effects, but without intoxicating or addictive properties), reduces illicit cannabis use in patients with CUD, warranting further research. This double-blind randomised controlled trial will compare CBD (400mg oral daily) versus placebo, in a 12-week outpatient intervention in 250 treatment-seeking participants with moderate or severe CUD and with no severe comorbidities. All participants will receive counselling and regular monitoring.

The primary outcome is a reduction in illicit cannabis use, measured by self-report (cannabis-free days) and urine drug screens. Secondary outcomes include (a) cannabis related harms; (b) adverse events; (c) mental and physical

health; (d) quality of life and social functioning; (e) other substance use (f) patient experience; (g) cognition and (h) cost effectiveness. We will review participants 12 weeks after the intervention (week 24) to assess persistence of post-treatment outcomes. A qualitative component amongst Aboriginal participants (predicted at 20% of total sample) will examine their treatment and research experiences. An intention to treat analysis will use multiple imputation to account for missing data.

The 4 year study will be conducted in specialist addiction services in NSW and Victoria, bringing together leading clinical research groups, consumer organisations and Aboriginal stakeholders, including Aboriginal researchers, health workers and consumers.

Research Team

Research Team			
Role	**Investigator**	**Primary Institution**	**Will CI be based in Australia?**
CIA	Prof Nicholas Lintzeris	University of Sydney	Yes

Relevant Background and Expertise:
NL is a senior clinician researcher with 30 years' experience in the Alcohol and other Drug field. NL is a Conjoint Professor in the Specialty of Addiction Medicine, University Sydney; Director of Drug & Alcohol Services at South Eastern Sydney Local Health District (since 2010), and practicing Addiction Medicine Specialist.

NL has an extensive research background (PhD, NHMRC post-doc fellowship) with $40M career grant funding and >200 peer review journal publications. NL's career research focus has been the development and implementation of pharmacotherapies for substance use disorders. NL has led numerous research studies, including 3 NHMRC funded RCTs for cannabis treatment as CIA and has been investigator on trials of medicinal cannabinoids for cannabis use disorder, alcohol withdrawal, palliative care, cancer chemotherapy, driving impairment, and health services research. NL is a CI on the NHMRC The Australian Centre for Cannabinoid Clinical and Research Excellence.

NL was the Foundation Chair of the NSW Drug & Alcohol Clinical Research and Improvement Network (DACRIN), an ACTA-affiliated clinical research network spanning the NSW Local Health Districts participating in this project, and a Board member of the National Centre Clinical Research into Emerging Drugs. NL is a leading clinician researcher in addiction treatment in Australia, frequently collaborating with the investigators, clinical and consumer organisations on this grant.

NL has considerable experience in policy (e.g. Chief Addiction Medicine Specialist for NSW Health 2011-13; current President Chapter of Addiction Medicine, Royal Australasian College Physicians), professional development, systematic reviews (e.g. Cochrane, Sax Institute) and clinical guideline development (e.g. author of national opioid and alcohol treatment guidelines). This breadth of clinical, research, professional development and policy work ideally positions NL to translate clinical research into practice.

CIB	Prof Daniel Lubman	Monash University	N/A

Relevant Background and Expertise:
DL trained as a Psychiatrist and Addiction Medicine Specialist. As Director of Turning Point and Professor of Addiction Studies at Monash University, DL heads Australia's leading national addiction treatment, research, and training centre, providing policy advice to government, national research programs and training courses, direct clinical care to patients and their families, including telephone-based programs across six jurisdictions, as well as national online alcohol, drug and gambling services.

DL's research is wide-ranging and includes investigating the impact of alcohol and drug use on brain function, the relationship between substance use and mental disorders as well as the development of targeted intervention programs within school, primary care, mental health and drug treatment settings. DL has led numerous studies examining the neurobiology of addiction, in both adolescent and adult populations, as well as multiple clinical trials examining the effectiveness of pharmacological and psychological approaches for substance use and co-occurring mental disorders. DL has led epidemiological work examining the relationship between substance use and mental illness and community responses, as well as a number of large cohort studies, including Patient Pathways, the largest Australian study of people accessing alcohol and drug treatment services. DL has also led the establishment of a national surveillance system for alcohol, drug, mental health, self-harm and suicide utilising ambulance attendances from across Australia.

DL has published >500 peer reviewed journal articles, major reports and book chapters, and has obtained >35 million dollars in research funding including 26 NHMRC and ARC grants.

CIC	Dr Michael Doyle	University of Sydney	N/A

Relevant Background and Expertise:
MD is a Bardi Aboriginal man from the Kimberley region of Western Australia. He is an early career researcher and Senior Research Fellow at the NHMRC Centre of Research Excellence in Indigenous Health and Alcohol, Sydney University. MD's PhD was completed in 2018. He was awarded a NHMRC Investigator grant emerging leader level

1 in 2020 (GNT1193618). Since 2018 MD has published 13 peer reviewed papers, six as first author, with another two first author papers currently under review. MD's alcohol and other drug (AoD) research uses mixed methods focusing on Aboriginal men and the criminal justice system. Having witnessed and experienced dysfunctional behaviour caused by problematic AoD use among the Bardi people and the broader Aboriginal and Torres Strait Islander community, MD is highly motivated to reduce the health harms and social impacts of AoD use through the delivery of evidence informed and culturally sensitive, treatment and support services. MD also works in prevention, and is CID on the Strong and Deadly Futures: A cluster randomised controlled trial of a computerised school-based alcohol and drug prevention program for Aboriginal and Torres Strait Islander students (GNT1163416). Strong and Deadly Futures incorporates lessons aimed at preventing cannabis use.

Throughout MD's career as an Aboriginal health worker in Aboriginal Community Controlled Health Services and as a researcher he has worked with the Aboriginal community and maintained strong community engagement. MD has been the acting chair of the Aboriginal Health and Medical Research Council of NSW Human Research Ethics Committee since March 2021. On this grant MD would help ensure appropriate Aboriginal community engagement and governance. The proposed Cannabis Use Disorder project will be a significant capacity building opportunity for MD to develop skills in the management of a clinical control trial.

CID	Prof Adrian Dunlop	Hunter New England Local Health District	N/A

Relevant Background and Expertise:
AD is an addiction medicine specialist and clinical researcher with 25 years experience in drug and alcohol treatment, research and policy. AD is Director and Senior Staff Specialist for Drug & Alcohol Clinical Services, Hunter New England Local Health District (since 2007) and Conjoint Professor, School of Medicine and Public Health, Faculty of Health, University of Newcastle. AD is a Foundation Fellow of the Australasian Chapter of Addiction Medicine and is current President-Elect of the Chapter Committee, and Past-President of the Australasian Professional Society on Alcohol and other Drugs (APSAD). AD was the Chief Addiction Medicine Specialist, Drug & Alcohol Branch, NSW Health (2014-2018).

AD has been an investigator in 50 research grants including over $A34 million in competitive research funding including 12 NHMRC funded grants (9 as CI), one ARC grant and one CRE grant. He is a foundation member of the NSW Drug and Alcohol Clinical Research Network, a collaboration of NSW public sector D&A Services engaged in clinical research. AD has collaborated on NHRMC funded studies of medications for cannabis withdrawal and dependence and methamphetamine dependence (one in Aboriginal communities), tobacco (NSW Health funded) and opioid dependence (NSW Health funded) including a study of depot buprenorphine in custodial settings (2018-19) that was rapidly translated into practice from the start of the COVID-19 pandemic, resulting in a significant increase in treatment uptake in prisons from 2020.

MD has over 132 peer reviewed publications and is a co-author on 9 Australian guidelines on drug and alcohol treatment management. MD is a Fellow of the International Society for Addiction Medicine, member of the College of Problems on Drug Dependence, Society for the Study of Addiction and was awarded a Churchill Fellowship (2005) to investigate opiate dependence in pregnancy. MD has been awarded the APSAD Senior Scientist Award, Clinician Award and been a James Rankin orator.

CIE	Dr Llewellyn Mills	University of Sydney	N/A

Relevant Background and Expertise:
LM is an early career researcher specialising in clinical addiction research. LM received their PhD in Psychology in February 2018 and since then has worked as a postdoctoral researcher for the Specialty of Addiction Medicine, University of Sydney and for South Eastern Sydney Local Health District Drug and Alcohol services. LM has co-authored 17 manuscripts in international peer reviewed journals, 14 in the area of substance abuse and dependence, and has presented their research at conferences around the world.

During their short career, LM has specialised in cannabis research, including (i) coordinating and leading data analysis on an NHMRC-funded, multisite, randomised controlled clinical trial testing the efficacy and safety of a THC:CBD drug, nabiximols, for treating cannabis dependence, (ii) coordinating and analysing data for an online survey recording the experiences of medical cannabis users in Australia, (iii) validating the Australian Treatment Outcomes Profile, a clinical health and wellbeing measurement tool used by NSW drug and alcohol treatment services, for use in people being treated for cannabis dependence.

LM's expertise is in data science and statistical methods, with advanced skills in experimental design and statistics

including longitudinal data analysis, multiple imputation, nonlinear regression, sample size calculation, Bayesian statistics, and machine learning. LM led data analysis on three NHMRC-funded randomised controlled trials and has been involved in projects that find ways to use routinely collected clinical data collected on electronic medical records to answer questions of practical importance to drug and alcohol clinicians. LM is currently the biostatistical consultant for the Drug and Alcohol Clinical Research and Improvement Network, an organisation comprised of clinical drug and alcohol researchers from around Australia, offering advice to stakeholders on sample size calculations, statistical analysis and experimental design.

CIF	Dr Mary Ellen Harrod	NSW User's & AIDS Association	N/A

Relevant Background and Expertise:
MH is the CEO of the NSW Users and AIDS Association a community-based drug organisation funded by NSW Health to provide services to and represent people who use or have used drugs in NSW. While at NUAA, MH has significantly increased NUAA's engagement with broader discussions around harm reduction and alcohol and other drug treatment services by bringing innovative, peer-led programs and services to NSW such as DanceWize NSW, the Consumers Guide to Opioid Treatment and the Peer and Consumer Forum.

MH has made extensive contributions to NSW and Australian policy discussions on harm reduction, blood borne virus treatment and prevention, drug policy reform and the alcohol and other drug treatment system. MH has provided critical input into a number of policy and strategy documents nationally and in NSW and represents consumers in key NSW committees such as the HIV Strategy Implementation Committee, Drug and Alcohol Program Council, the NSW Music Festival Roundtable and the OTP Expert Advisory Committee to name a few.

MH has successfully participated in several funded research grants while at NUAA including acting as a Chief Investigator on the NSW Health funded ORTHN study and the NHMRC funded ETHOS and TEMPO studies. MH has an extensive background as a public health researcher with previous roles including clinical project leader of a NHMRC funded CRE working with Aboriginal Community Controlled Health Services across Australia. A number of the projects MH has collaborated on have been translated into clinical settings including service level changes at several ACCHOs and statewide implementation of naloxone.

MH has over 20 peer-reviewed publications and has appeared at numerous national and international conferences. MH has a strong record of public advocacy and community engagement having served on the Board of other community harm reduction and drug user organisations and appeared as an invited speaker in multiple forums.

CIG	Dr Shalini Arunogiri	Monash University	N/A

Relevant Background and Expertise:
SA is a clinical addiction psychiatrist and early career clinician- researcher and is Deputy Head of the Department of Psychiatry at Central Clinical School, Monash University, and leads the Addiction Research Program at MAPrc (Monash Alfred Psychiatry Research Centre). Clinically, SA is Deputy Clinical Director at Turning Point, Eastern Health, a national treatment centre offering outpatient, inpatient, telephone and online addiction treatment to over 100,000 people annually.

SA has an exemplary track record relative to career stage and opportunity. SA has attracted over $8M NHMRC funding as a CI on three current RCTs in substance use disorder and has over 40 peer-reviewed publications to date. SA held an NHMRC Postgraduate Scholarship during their PhD (2015-2018), and has been awarded a number of prestigious awards and early career grants (Society for Mental Health ECR Grant 2018; College on Problems of Drug Dependence CPDD/NIDA Women and Sex/Gender Junior Investigator Travel Award 2020).

SA brings considerable experience in recruiting addiction treatment-seekers into clinical trials. SA's PhD examined cognitive correlates of methamphetamine-associated psychosis, recruiting 120 methamphetamine-using participants from community and clinical settings. SA held investigator roles on the only Victorian site of two clinical trials for methamphetamine use disorder (LiMA Lisdexamfetamine; and N-ICE N-Acetylcysteine), and also recruited into a CI-A funded study on cognitive markers of aggression in methamphetamine use. Collectively, these studies established recruitment pipelines attracting over 300+ individuals with substance use disorder.

CIH	Assoc Prof Peter Malouf	University of Sydney	N/A

Relevant Background and Expertise:
PM is proud Wakka Wakka and Wulli Wulli, academic, epidemiologist, and executive director at the Aboriginal Health and Medical Research Council for NSW.

PM's academic outputs include >6 peer-reviewed publications with >120 citations and an h-index of 3, i10-index 2. Top h-index cited (>75 citations): Cortisol Awakening Response in Patients with Psychosis: Systematic Review and Meta-Analysis, Neuroscience & Biobehavioral Reviews.
PM has an Honorary Associate Professorial Fellow, Ngarruwan Ngadju First Nations Research Centre, Australian Health Services Research Institute, University of Wollongong, and holds an Adjunct Associate Professor role at Sydney Medical School, University of Sydney.

PM is CI-C on an NSW Ministry of Health, COVID-19 research grant ($790,000), a place-based pandemic response to the strengths and vulnerabilities of Aboriginal communities in south-eastern New South Wales, attracting 15% credit share to SMS ($15,000). PM is currently a CI(B) on a Review of the Integrated Team Care Primary Health Network program in South Eastern New South Wales ($120,000), funded through the Primary Health Network March 2020 - February 2021, attracting 30% credit share to SMS ($26,000). Recently PM has been AI on an Indigenous-led evaluation of Aboriginal Programs funded by the Sax Institute, Indigenous Health Research Fund Medical Research Future Fund ($1.3millon).

CII	Prof Paul Haber	Royal Prince Alfred Hospital	N/A

Relevant Background and Expertise:
PH is a physician in gastroenterology and addiction medicine and clinical researcher with 30 years' experience in drug and alcohol treatment, research, and policy. PH is Director and Senior Staff Specialist for Drug & Alcohol Clinical Services, Sydney Local Health District, and Foundation Professor in the Specialty of Addiction Medicine, Sydney Medical School, University of Sydney. PH is a Foundation Fellow and past President of the Australasian Chapter of Addiction Medicine (RACP). He was Clinical Advisor in Addiction Medicine to NSW Health (2012-2014) and co-founder of the Drug and Alcohol Clinical Research Network (DACRIN).

PH has been an investigator in research grants including over $A34 million in competitive research funding with continuous NHMRC funding since 1996 across 21 grants as CI, including three CRE grants and three NIH grants. PH has led and collaborated on clinical trials of treatment for alcohol use disorder, medications for cannabis withdrawal and dependence and methamphetamine dependence (NHMRC funded), tobacco (NSW Health funded) and opioid dependence (NSW Health funded) including studies of depot buprenorphine in community settings and custodial settings (2018-19).

PH has authored 247 peer reviewed publications (23 with >100 citations), 6 books and led Australian guidelines on alcohol treatment and contributed to others. PH is a Fellow and past Board member of the International Society for Addiction Medicine amongst other Societies and was awarded a NHMRC Practitioner Research Fellowships in 2008 and 2019. PH has been awarded the APSAD Senior Scientist Award and a Member of the Order of Australia (AM) in 2019.

CIJ	Assoc Prof Tom Freeman	University of Bath	N/A

Relevant Background and Expertise:
TF is an Associate Professor and Director of the Addiction and Mental Health Group at the University of Bath, UK and is a leading international author of cannabis research and has considerable experience in experimental and clinical trials of CBD. In the past five years, TF received 3.5 million GBP and 2.5 million EUR in research funding (approximately 10 million AUD) primarily focusing on cannabis and cannabinoids.

TF recently led the first randomised clinical trial of CBD for cannabis use disorder in an adaptive phase 2a Bayesian dose-finding trial. This trial identified 400mg as the most efficacious dose for reducing cannabis use with no increase in adverse events compared to placebo. TF has conducted extensive work in the past 5 years characterising how THC and CBD concentrations have changed in cannabis over time, and their relationship with cannabis use disorder and its treatment.

TF is internationally known for his research on cannabis use measurement, including the development of the standard THC unit which has gained support and prompted subsequent work by Nora Volkow, Director of the National Institute on Drug Abuse, USA. TF is an elected member of Council for the British Association for Psychopharmacology and was supported by the Society for the Study of Addiction on a Griffith Edwards Senior Academic Fellowship. TF contributed to the first National Institute for Health and Care Excellence (NICE) guidelines on cannabis-based medicines as an expert witness in Cannabinoid Psychopharmacology and has been commissioned to work on a series of projects for the European Union drugs agency focusing on cannabis.

Associate Investigators		
Name	**Primary Institution**	**Position**
Prof Nadia Solowij	University of Wollongong	Co-Director Australian Centre for Cannabinoid Clinical and Research Excellence

Relevant Background and Expertise:
NS (PhD) is a Professor in the School of Psychology at the University of Wollongong and Co-Director of the Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE), an NHMRC Centre of Research Excellence. NS has been engaged in cannabis research for 30 years, with extensive experience in all aspects of cannabis research in humans, including clinical and neuropsychological assessment, brain electrophysiology and brain imaging. NS is the most published author in the world in the area of cannabis, cognition and the brain (Web of Science) with more than 200 publications in total, many of these highly cited.

NS has been CIA on four NHMRC project grants (one current), CIB on two others (both current) and CIB (Co-Director) on the NHMRC Centre of Research Excellence (ACRE; current), as well as the Principal Investigator on several large competitively funded projects managing large teams of researchers. Recently NS has overseen an NHMRC-funded randomised controlled trial of cannabinoid administration to humans, and as a part of an ARC Future Fellowship, pursued a broad program of research to understand further the effects of cannabis on the brain, including a trial of prolonged CBD administration to cannabis users – of direct relevance to this proposal.

NS will contribute their knowledge and expertise to this project in psychopharmacology and the pharmacology of cannabis, neuropsychology, cognition and psychopathology as pertinent to cannabis, and in particular her experience in running CBD trials. As a world leader in these areas, NS will work closely with the team to ensure the success of the project and wide ranging dissemination of its findings.

Robert Graham		Director of Western Sydney LHD Drug Hea;th

Relevant Background and Expertise:
RG is the director of Western Sydney Local Health District (WSLHD) Drug Health, a staff specialist in Addiction Medicine and manages a service of over 100 staff of various clinical, research and administrative disciplines.

RG has 20 years experience in clinical research and treatment in disorders involving cannabis, opioids, alcohol and methamphetamine use. RG has experience in leading clinical trials as a local PI which comply with International Conference Harmonization and Good Clinical Practice (ICH/GCP) requirements in relevant to clinical research in substance use disorders.

RG has experience in leading the clinical studies, liaising with site staff and investigators to ensure the study will be conducted according to (ICH/GCP) and approved protocol requirements. Besides their director role, RG is also involved in implementing the clinical research, leading staff (including managing the local research team) and participant recruitment and consent for these studies at Drug Health.

RG has publications, conference presentations and past surveyor for the Chapter of Addiction Medicine. is a member of the NSW Drug and Alcohol Clinical Research Network, a collaboration of statewide D&A Services.

Besides participating in multisite clinical research, RG is also establishing clinical trials in WSLHD such as a novel management of opioid dependence. Recently, RG implemented an outbreak management plan in the Drug Health Service and also has initiated clinical research in COVID-19 with local researchers.

Steven Childs	Central Coast Local Health District	Manager Drug and Alcohol Services, Central Coast LHD

Relevant Background and Expertise:
SC (BA, LLB, M. Appl. Psychol, MAPS) is a psychologist and Manager of Central Coast Local Health District (CCLHD) Drug and Alcohol Service and HIV and related Programs. SC has over 25 years' experience in the addictions field as a clinician and clinical manager who has supported and participated in research. In this position SC oversees a department of over 80 people including psychologists, social workers, nursing, health promotion and medical.

SC was the clinical manager that established the Central Coast Cannabis Clinic in 2004 and oversaw the

development of the model of care for the clinic. SC has participated as a member on numerous NSW Health Committees including the Cannabis Working Party, MERIT Advisory Committee, Quality in Treatment Committee and Drug and Alcohol Program Council. He is currently co-chair of the expert group reviewing the NSW, D&A Psychosocial Professional Practice Guidelines.

SC has co-authored papers on self-compassion, therapeutic alliance, and computerised psychological treatment and also contributed to the first paper to describe the NSW Drug and Alcohol Aboriginal Workforce and a chapter in the Handbook for Aboriginal Alcohol and Drug Work 2012.

SC will contribute to the project by overseeing the counselling portion of the treatment interventions and ensuring that treatments are standardised across sites and treatment arms. SC will also have input into protocol composition and, as manager of Central Coast LHD, will be responsible for monitoring protocol compliance at that site. Lastly SC will be involved in manuscript composition and editing.

Steve Ella	Central Coast Local Health District	Manager of Nunyara Aboriginal Health Unit, Central Coast LHD

Relevant Background and Expertise:
SE is an Aboriginal man from the Yuin Nation on the South Coast of NSW. SE is the Manager of Nunyara Aboriginal Health Unit for the Central Coast Local Health District, and has a 20 year background in Aboriginal Drug and Alcohol work on the Central Coast and state wide. He was inducted into the National Indigenous Drug and Alcohol Honour Roll in 2012 at the National Indigenous Drug Alcohol conference in Fremantle, and was awarded the First Peoples award at the Australasian Professional Society on Alcohol and other Drugs (APSAD) conference in Brisbane in 2013. SE has co-authored a handbook for Aboriginal Alcohol and Drug Work and has been award the Master of Philosophy via research by investigating the Aboriginal Drug and Alcohol workforce which assisted SE to be an Associate Investigator with the Centre of Research Excellence- Indigenous Health and Alcohol Research

SE has been working in the Aboriginal Drug and Alcohol industry from 1916 to 2016 at Central Coast Local Health district. Other the 20 year period, Steve provided ongoing support for Aboriginal cannabis users from initial support through services such as Detoxification to rehabilitation centres or Counselling through the Cannabis clinic in which Steve was Manager.

SE has extensive experience working in Aboriginal communities, the initial 20 years as the Aboriginal drug and Alcohol consultant, 6 years as the state wide Aboriginal Drug and Alcohol traineeship Coordinator as well as Manager of the Counselling and Cannabis clinic teams within the Drug and Alcohol service. Steve is now the current Manager of the Aboriginal Health Unit for the Central Coast Local Health District.

SE was also instrumental in the development of the Aboriginal Drug & Alcohol Network (ADAN) and ADAN Leadership group which he chaired for a number of years. This is the lead committee for Aboriginal drug and Alcohol work in NSW.

Dr Mark Montebello	University of Sydney	Clinical Director, Northern Sydney LHD

Relevant Background and Expertise:
MM is a psychiatrist, addiction medicine specialist and clinical researcher with 20 years' experience in drug and alcohol treatment, research and workforce development. MM is the Clinical Director and Senior Staff Specialist for the Northern Sydney Local Health District Drug and Alcohol Service; Honorary Senior Lecturer, National Drug and Alcohol Research Centre, University of New South Wales; Clinical Senior Lecturer, Specialty of Addiction Medicine, University of Sydney; and Member of the Advisory Board for the Australian and New Zealand Journal of Psychiatry. MM's research interests include randomised controlled trials of novel treatment interventions for substance use disorders, co-morbidity with mental health disorders and treatment of Hepatitis C Virus in drug and alcohol settings. MM has worked with diverse research consortia including the Agonist Replacement for Cannabis Dependence (ARCD) study group and Drug and Alcohol Clinical Research and Improvement Network (DACRIN). MM was an AI on the NHMRC funded trial - 'An RCT of cannabinoid replacement therapy (Sativex®) for the management of treatment-resistant cannabis dependent patients' and was an author on papers arising from this trial.

MM has also been involved in clinical trials investigating the effects of mirtazapine, rimonabant and exercise in the treatment of cannabis dependence. MM has been an investigator in 28 research grants including 6 NHMRC

funded grants and has 18 peer reviewed publications. In 2019, MM was awarded the Australasian Professional Society on Alcohol and other Drugs Clinician of the Year Award.
Roles in this trial includes carriage and stewardship of the project within Northern Sydney Local Health District Drug and Alcohol Service including input into trial design; facilitating NSLHD Research Governance Office approval; assistance with the recruitment of trial participants; ongoing monitoring of standards; contribution to data analysis; and preparation of publications.

Martin Nean	Hunter New England Local Health District	Chairperson, Aboriginal Drug and Alcohol Network (ADAN)

Relevant Background and Expertise:
MN is an Aboriginal man from the Gomeroi Nation in North West NSW who has a strong connection to country and mob. MN is the current Manager of the Aboriginal Drug and Alcohol Clinical Service for the Hunter New England Local Health District and has held this position for fourteen years. The key role of which is to develop, implement and maintain linkages with relevant stakeholders and the Aboriginal community by ensuring services are culturally sensitive, and competent.

Prior to working in the drug and alcohol industry, MN had 25 years' experience in Aboriginal Health as both an Aboriginal Health Worker and Manager. Martin has extensive knowledge and experience in working with Aboriginal communities across the Local Health District to improve service access and delivery as well as quality of life.

MN has been a member of the Aboriginal Drug & Alcohol Network (ADAN) for 14 years and is the current Chairperson – a position he has held for 11 years. During this time MN has steered the Network from existing as a program of the Aboriginal Health & Medical Research Committee to become the peak body for the Aboriginal drug and alcohol sector within NSW and offers a strong voice and important integrative functions to stakeholders. MN has received the 'Outstanding Commitment' award and been inducted into the Honour Roll.

Over the course of 35 years MN has, and continues to, present papers for Aboriginal Health as well as Drug and Alcohol at regional, state and national conferences.

Dr Peter Galettis	The University of Newcastle	Head of Clinical Pharmacology Laboratory, University of Newcastle

Relevant Background and Expertise:
PG is the Head of the Clinical Pharmacology Laboratory at the University of Newcastle and one of Australia's leading drug analysts. PG completed a BSc (Hons) in Biochemistry at the University of NSW (1987) before completing a PhD in Clinical Pharmacology at the University of Technology, Sydney (1997). PG's research interests are entirely within the field of clinical pharmacology and toxicology, where PG has specialised in assay development for use in drug monitoring for the last 30 years, with a particular focus on anticancer agents and drugs of abuse. PG's experience in pharmacology spans three decades, and includes both the preclinical (cell cytotoxicity assays, synergy experiments, animal models, animal pharmacokinetics) and clinical (translating preclinical combinations to clinical studies, pharmacokinetic studies, Phase I clinical trials, Phase II trials) settings. PG has established numerous analytical assays for the analysis of drugs using HPLC, LCMSMS and GCMS, and has been extensively involved in cannabis research over the last five years, and in the role of investigator, undertakes a majority of the pharmacokinetics work for the Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE), an NHMRC-funded Centre of Research Excellence; the NSW Health-funded Clinical Cannabis Medicines Program; and the CRC-P Project 'Growing the medicinal cannabis industry – precision farming to pharmaceuticals'. PG is also extensively involved as the pharmacokinetic lead on several other investigator and industry-led national medicinal cannabis clinical trials and studies including studies on CBD with Al Solowij. PG's role within this project will be advising on best practice for collection and analysis of biological samples.

Dr Penny Reeves	Hunter Medical Research Institute	Associate Director, Health Economics Unit, Hunter Medical Research Institute

Relevant Background and Expertise:
PR has over 20 years' experience in the field of applied health economics. PR is currently the acting Associate Director for the Health Research Economics unit at the Hunter Medical Research Institute (HMRI) where PR has

been employed for the last 7 years. Prior to being appointed at HMRI, PR held senior economist positions in industry and in government both in Australia and the UK. PR has led submissions to the Pharmaceutical Benefits Advisory Committee and Medical Services Advisory Committee. In PR's current role, specific areas of research interest include applied economic evaluation, the economics of implementation and health and medical research impact assessment. Under PR's leadership the HRE unit have advanced the development and application of research impact assessment. PR is a regular advisor to the Centre for Epidemiology and Evidence and Office of Health and Medical Research within NSW Health, and is also part of a national steering group leading innovation in improving the value of healthcare expenditure via the application of economic evaluation to support local level decision making.

PR has a PhD in Health Economics, a graduate diploma in Health Economics (University of Tromso, Norway) and a Bachelor of Economics (honours). Between July 2018 and September 2020, PR held a NSW Health Prevention Research Support Program (PRSP) funded research fellowship.

Dr Lauren Monds	University of Sydney	Research Coordinator, Drug and Alcohol Services, Northern Sydney LHD

Relevant Background and Expertise:
LM (BSc (Hons I), PhD 2013) holds a research and teaching position as a Lecturer in the Specialty of Addiction Medicine, Faculty of Medicine and Health, University of Sydney. LM also the Research Coordinator of the Drug and Alcohol Service at Northern Sydney Local Health District (one of the study sites), a senior leadership role focused on facilitating the growth of clinical research at that site. LM has combined her PhD research on memory with postdoctoral research on substance use disorder to lead an independent research program with a focus on cognitive impairment in substance using populations, including people who use cannabinoids. LM supervises a team of PhD students, honours students and research assistants. LM has successfully coordinated several large multi-site studies and clinical trials in substance use populations. LM's research has attracted >$450k in funding and has published over 30 in international, peer-reviewed journals including PNAS and Psychopharmacology. Despite being relatively early in their career, LM's translational research has already contributed to policy and practice change as evidenced by recommendations being adopted by the Ministry of Health, and a NSW Health South Eastern Sydney LHD Improvement and Innovation award for a NSW Health Translational Research Grant on responding to opioid overdose, that LM was an investigator on and the coordinator for. LM has also received multiple invitations to provide training workshops to government audiences such as NSW Health, the Australian Federal Police, and the West-Midlands Police (UK), workshps based on LM's own research. LM is regularly approached to provide expert witness reports for court cases involving alcohol and other drug intoxication and memory. LM will contribute expertise on the cognitive testing component of the study and will help facilitate and as Research Coordinator oversee study recruitment at North Sydney LHD Drug and Alcohol Service sites.

Dr Meryem Jefferies	Research Officer, Western Sydney LHD

Relevant Background and Expertise:
MJ has over 18 years experience in clinical research including addiction, therapeutics, vaccine and diagnostics development, has completed degrees in Nursing and veterinary science and holds a PhD in Medicine.

MJ is currently Research Officer at Western Sydney Local Health District (WSLHD) and has experience in all aspects of the day to day job of conducting clinical addiction research, including patient recruitment, conducting research interviews, venipuncture, collecting samples, liasing with participants, doctors, nurses, physiologists, pharmacists, and collecting and entering data. Most recently MJ was the chief research officer at WSLHD during the randomised controlled trial testing the efficacy of the cannabis agonist drug nabiximols for treatment of cannabis dependence. During this trial MJ ensured the trial was compliant with the mnethods contained in the trial protocol and was conducted in line with guidelines for Good Clinical Practice (GCP) outlined during the International Conference on Harmonisation Good Clinical Practice (ICH-GCP). MJ also has considerable experience training staff to ensure all research is conducted according to GCP principles and compliant with all health and safety policies of NSW Health.

MJ also has considerable experience with the dissemination of research findings, co-authoring 10 publcations in addiction, three dealing with Treatment of Cannabis Dependence.

MJ is currently establishing new projects in Harm minimization and impact of COVID-19 to Drug Health patients.

Total Budget Summary

Total Budget Summary					
Summary of Total 'Salary' per year					
Year 1 ($)	**Year 2 ($)**	**Year 3 ($)**	**Year 4 ($)**	**Year 5 ($)**	**Total Salary ($)**
$212,983	$801,420	$541,740	$81,570		$1,637,713
Summary of total 'Other Research Costs' (ORC) per year					
Year 1 ($)	**Year 2 ($)**	**Year 3 ($)**	**Year 4 ($)**	**Year 5 ($)**	**Total ORC ($)**
$35,715	$303,033	$126,777	$16,900		$482,425
Summary of total 'Equipment' per year					
Year 1 ($)	**Year 2 ($)**	**Year 3 ($)**	**Year 4 ($)**	**Year 5 ($)**	**Total Equipment ($)**
$	$	$	$		$
Total Requested Budget					
Year 1 ($)	**Year 2 ($)**	**Year 3 ($)**	**Year 4 ($)**	**Year 5 ($)**	**Total Budget ($)**
$248,698	$1,104,453	$668,517	$98,470		$2,120,138

Salary Request Summary

Salary Request Summary						
Position Function	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total**
Trial Coordinator PSP4	$94,666	$94,666	$94,666	$47,333		**$331,331**
	100%	100%	100%	50%		
Aboriginal Research Coordinator PSP4	$18,933	$18,933	$18,933	$9,467		**$66,266**
	20%	20%	20%	10%		
Site 1 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		
Site 2 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		
Site 3 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		
Site 4 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		
Site 5 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		
Site 6 research coordinator PSP3	$9,618	$40,074	$30,456	$		**$80,148**
	12%	50%	38%	0%		

Site 7 research coordinator PSP3	$9,618 12%	$40,074 50%	$30,456 38%	$ 0%	**$80,148**
Site 1 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 2 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 3 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 4 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 5 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 6 Research Nurse PSP3	$ 0%	$40,074 50%	$20,037 25%	$ 0%	**$60,111**
Site 7 Research Nurse PSP3	$ 0%	$32,059 40%	$16,030 20%	$ 0%	**$48,089**
Consumer (Peer) Researcher PSP2	$14,578 20%	$14,578 20%	$14,578 20%	$7,289 10%	**$51,022**
Trial Statistician PSP3	$8,015 10%	$8,015 10%	$8,015 10%	$8,015 10%	**$32,059**
Site 1 Aboriginal Health Worker PSP3	$ 0%	$16,030 20%	$8,015 10%	$ 0%	**$24,044**
Site 2 Aboriginal Health Worker PSP3	$ 0%	$16,030 20%	$8,015 10%	$ 0%	**$24,044**
Site 3 Aboriginal Health Worker PSP3	$ 0%	$16,030 20%	$8,015 10%	$ 0%	**$24,044**
Site 4 Aboriginal Health Worker PSP3	$ 0%	$16,030 20%	$8,015 10%	$ 0%	**$24,044**
Site 5 Aboriginal Health Worker	$	$16,030	$8,015	$	**$24,044**

PSP3	0%	20%	10%	0%	
Site 6 Aboriginal Health Worker	$	$16,030	$8,015	$	**$24,044**
PSP3	0%	20%	10%	0%	
Site 7 Aboriginal Health Worker	$	$16,030	$8,015	$	**$24,044**
PSP3	0%	20%	10%	0%	
Specialist Research Support	$9,467	$	$	$9,467	**$18,933**
PSP4	10%	0%	0%	10%	
	$212,983	**$801,420**	**$541,740**	**$81,570**	**$1,637,713**

Salary Request

Salary Request	
Position Function	**Justification**
Trial Coordinator PSP4	A full time Trial Coordinator is required for the duration of the project to manage this complex RCT across 7 sites in 2 states. Duties will include planning and organisation of the study, including co-ordination of ethics and other research governance (e.g. CTRAs, progress reports to funders, sponsor, ethics, drug company); maintaining Project Steering Committee over the duration of the project; writing study protocol, operating procedures and CRFs in consultation with the CI team; recruitment, training and supervision of site research co-ordinators; monitoring of participant recruitment; establishment of study data bases, 6-monthly monitoring of data collection at each site, co-ordination of data cleaning; archiving study records; liaison with study statistician, health economist and investigators in data analysis, write up and dissemination activities. A postdoctoral researcher with prior experience in coordinating clinical trials is required – consistent with PSP4 level.
Aboriginal Research Coordinator PSP4	This Aboriginal Research Coordinator will work alongside the Full-time Trial co-ordinator and focus on ensuring activities relating to community engagement, recruitment, intervention design, supervision of Aboriginal Health workers on the project and coordination of the Aboriginal Governance Group, qualitiative research interveiews and analysis (along with CI-Doyle), and will lead any sub-analyses that relate to Aboriginal analyses, write up and dissemination back to communities are led by the Aboriginal researcher, together with CI-Doyle and Malouf. The position will be for a candidate of Aboriginal or Torres Strait Islander background of suitable qualifications (consistent with PSP4), who will be given on-the-job training and supervision by the trial coordinator in order to increase the pool of qualified Indigenous clinical drug and alcohol research trial coordinators.
Site 1 research coordinator PSP3	Position is for trial site 1 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up

	An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 2 research coordinator PSP3	Position is for trial site 2 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 3 research coordinator PSP3	Position is for trial site 3 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 4 research coordinator PSP3	Position is for trial site 4 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 5 research coordinator PSP3	Position is for trial site 5 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28

	participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 6 research coordinator PSP3	Position is for trial site 6 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 7 research coordinator PSP3	Position is for trial site 7 at 50% FTE for 24 months: starting 3 months prior to site initiation (end Year 1), for the participant recruitment and follow-up (18 months), and for further 3 months to finalise data entry and site closure. With the local Site Investigator, the position will - coordinate local research governance (e.g. ethics, GCP requirements) and reporting - implement and coordinate study clinical (e.g. pathology, pharmacy) and research procedures (- coordinate recruitment and screening of ~28 participants over 12 months, in liaison with clinical teams - conduct research participant interviews (5 interviews per participant, with ~28 participants per site – amounting to 140 interviews over 18 months) - data entry, assistance in data monitoring and data clean up An experienced graduate research assistant / junior postdoctoral researcher with data management and high level communication skills consistent with PSP3 is required to coordinate activities at each site.
Site 1 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 1. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 2 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 2. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g.

	medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 3 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 3. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 4 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 4. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2 days per week (40%) reflects a case load of ~4 to 6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 5 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 5. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 6 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 6. The position requires a nurse with research and specialist Drug and Alcohol skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Site 7 Research Nurse PSP3	The position is for the 18 months of clinical activity (recruitment, treatment) at site 7. The position requires a nurse with research and specialist Drug and Alcohol

	skills (consistent with PSP 3) who will act as the local nursing and clinical co-ordinator, liaising with other clinical staff (Medical Officer, psychologists, pharmacists) and research staff to attend to research related clinical activities beyond routine care. These include facilitating screening and recruitment, regular clinical reviews of participants, study pathology handling (e.g. UDS, bloods), clinical case report form data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. Whilst many aspects of the study intervention are provided by local health services (e.g. medical, psychology), this position, at 2.5 days per week (50%) reflects a case load of ~6 participants at any one time in treatment, and is critical in implementing the study at each site.
Consumer (Peer) Researcher PSP2	The consumer / peer research is scheduled at 1 day per week (20%) over 3.5 years to co-odinate consumer activities across the 7 sites. Activities include study planning (finalisation of procedures, participant information, recruitment strategy and trial promotion activities through relevant consumer organisations, assist in staff training), to participate in co-ordination throughout the project (Project Steering Committee member) including the coordination of the Consumer Advisory Group for the project, to assist with recruitment and participant research follow-up strategies, and coordination of dissemination of findings to consumers. Many individuals with substance use backgrounds struggle with engaging with health services and research trials in particular, and the importance of consumer engagement through peer workers is increasingly recognised. The position requires an individual with experience working in consumer organisations and research projects, consistent with PSP 2.
Trial Statistician PSP3	Position is for trial statistician at 10% FTE for 48 months. The trial statistician will be required to provide ongoing statistical support for the duration of the trial. At the outset this will include composing a detailed statistical analysis plan for trial protocol and ethics applications, and offering advice on data collection through the REDCap survey software and data repository. Continual data monitoring from the different sites will be performed throughout the trial to ensure data quality is being maintained as well as interim descriptive statistical analysis. The bulk of work will be at the close of the trial with data cleaning (including querying missing or incorrect data entry), preparation of datasets, constructing shell tables, running all analysis, reporting results to investigators, and composing manuscripts and data visualisations for conference presentations. Candidate will have a post-graduate qualification in quantitative statistical analysis, consistent with PSP3.
Site 1 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 1. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Site 2 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 2. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the

	Research Nurse at each site with screening recruitment, clinical reviews, pathology, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Site 3 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 3. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Site 4 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 4. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Site 5 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 5. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, data collection and entry, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Site 6 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 6. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.

Site 7 Aboriginal Health Worker PSP3	The position is for the 18 months of specialist clinical activity (recruitment, treatment) with participants of Aboriginal and/or Torres Strait Islander descent and their community at site 7. The position requires a health worker of Aboriginal and/or Torres Strait Islander descent who holds a relevant qualification in Aboriginal Health (e.g. Cert III Aboriginal Primary Health Care) and has experience in Drug and Alcohol treatment, consistent with PSP 3. The applicant will work under the Aboriginal Research Coordinator to liaise with the Aboriginal and/or Torres Strait Islander participants at each site and their families and will assist the Research Nurse at each site with screening recruitment, clinical reviews, pathology, assistance with data monitoring, and coordinating site clinical research meetings. At 1 day per week (20%, ~2 to 3 participants at any one time in treatment) this position is critical in implementing the study at each site.
Specialist Research Support PSP4	Specialist research support will be required to refine the Bayesian optimal dose estimation analysis conducted in CIJ's pilot study (see Statistical Analysis section of Proposal). Bayesian analyses allow for results from one study to inform shape and locations of prior distributions in subsequent studies, thus effectively integrating information across studies. These analyses are typically highly specialised and beyond the scope of most clinical trial biostatisticians, and hence will be required in addition to the trial statistician. Participation in finalisation of data collection procedures, model development, specification and write up of results as per methods. The span over 4 years reflecting involvement in study establishment during Year 1, and with data analysis and write up in Year 4. Successful candidate will have experience with Bayesian optimal dose estimation procedures and hold a post-graduate qualification in mathematical statistics, consistent with PSP4.

Other Research Costs Summary

Other Research Costs Summary						
Item	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total**
Health ecomonist	$10,000	$5,000	$20,000	$15,000		**$50,000**
Trial pharmacy expenses	$19,065	$82,033	$26,702	$0		**$127,800**
Pathology: Urine analyses for cannabis use	$0	$129,500	$55,500	$0		**$185,000**
Pathology: liver function and other blood tests	$0	$20,125	$8,625	$0		**$28,750**
Participant reimbursement	$0	$50,000	$12,500	$0		**$62,500**
Point of Care Urine Tests	$0	$6,975	$0	$0		**$6,975**
Travel and accomodation	$6,650	$1,900	$950	$1,900		**$11,400**
Trial recruitment strategies	$0	$2,500	$0	$0		**$2,500**
Drug Safety Monitoring Board expenses	$0	$5,000	$2,500	$0		**$7,500**
	$35,715	**$303,033**	**$126,777**	**$16,900**		**$482,425**

Other Research Costs

Other Research Costs	
Item	**Justification**

Other Research Costs	
Item	**Justification**
Health ecomonist	Health economic evaluation conducted by experienced economist from Hunter Medical Research Institute which is a cost recovery unit. Quote includes participation in finalisation of study and procedures, model development, specification and write up of results as per methods. The span over 4 years reflects involvement in study establishment (year 1), with emphasis upon data analysis and write up in Years 3 and 4.
Trial pharmacy expenses	Expenses based on Clinical Trial Drug Fees of the the NSW Association of Directors of Pharmacy (a) Administration at each site include Establishment $1800 + (admin + storage @$2,100 p.a. x 1.5 yrs) + close up $450 = $5,400 per site, with 7 sites = $37,800. (b) Medication dispensing fees involve 6 dispensing episodes (at weeks 0, 2, 4, 6, 8, & 10) per participant x $60 dispensing fee x 250 participants = $90,000. Total = $127,800. Medication not included: provided separately by GW Pharmaceuticals
Pathology: Urine analyses for cannabis use	Biological assessment of recent cannabis use is best with LCMS quantification of THC-COOH levels (creatinine adjusted). Samples collected weeks 0, 2, 4, 6, 8, 10, 12, and 24. The cost of LCMS analysis of THC-COOH by RPAH Laboratory (Sydney) is $54 per sample. NSW Health Pathology charge $35 per sample for processing and cold storage = $89 per sample. $89 per participant x 8 samples x 250 participants = $178,00. plus $1,000 courier fees per site (x7) to transfer samples to RPAH. Total = $185,000.
Pathology: liver function and other blood tests	Blood samples will be collected at baseline and Week 12 for safety assessments (liver function tests, full blood count) ~325 participants (to recruit 250) at baseline, 250 at week 12 = 575 samples. Cost of collecting and anlaysis of samples = $50 each, with each sample handled at local pathology services. Total cost = 575 x $50 = $28,750, with majority (70%) in Year 2.
Participant reimbursement	Reimbursement of participant expenses in attending research interviews (5 each over the course of the study). This is a key strategy for ensuring high research follow-up rates, recognising and compensating particpants for the inconvenience of lengthy research interviews and biological sampling (urine tests). Each interview is reimbursed at a rate of $50, consistent with previous research by the DACRIN research network. 250 x 5 x $50 = $62,500
Point of Care Urine Tests	Point of care urine tests will be used during screening for eligibility, and will include urine drug test (to confirm recent cannabis use), and to test for pregnancy (beta-hCG) in women. We estimate 325 clients will be screened for eligibility (all tested for urine drug screen), of which 40% (130, based on previous cannabis treatment studies) will be women (requiring beta-hCG). Each PoC urine test costs $15, with 465 tests = $6,975, and will be used during the recruitment phase (year 2)
Travel and accomodation	Travel Sydney - Melbourne - study establishment (training, site initiation): CIA, project co-ordinators (trial, consumer and Aboriginal) & Al-Childs (CBT training). 5 trips Year 1 - Data monitoring by Trial coordinator. 2 trips Year 2, 1 trip Year 3 - Face to face Investigator meeting Year 1 and Year 4. Melbourne investigators (CI-Lubman, Arunogiri) travel to Sydney. 2 trips Year 1, 2 trips year 4 Each Syd-Melb return flight, 1 night accommodation, travel to airport = $950. 12 x $950= $11,400
Trial recruitment strategies	Recruitment strategies will include social media (e.g. facebook), trial recruitment platforms and other advertising costs. All recruitment strategies to be submitted and approved by ethics committee. Costs based on previous studies targeting cannabis users by this research group.
Drug Safety Monitoring Board expenses	Costs associated with establishing and maintaining DSMB, including payment of independent statistician and clinical experts, and any associated expenses (catering, travel). Allow $2,500 per meeting x 3 meetings

Equipment Request Summary

Equipment Request Summary						
Item	Year 1	Year 2	Year 3	Year 4	Year 5	Total
	$	$	$	$		$

Equipment Request

Equipment Request	
Item	Justification