ACRE
Australian Centre for Cannabinoid Clinical and Research Excellence

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

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Centre for Drug Repurposing and Medicines Research
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An Overview of ACRE

- Australia's first federally-funded research centre focused on medicinal cannabinoids (2017 – 2022)
- Incorporates 20+ Chief and Associate Investigators from multi-disciplinary fields (e.g. pharmacology; clinical psychology; plant science; public health; health economics) across 10 Universities
- Strategic aims include a well governed collaborative strategy to generate evidence base and clinical guidance through world class research

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Development of Future Capacity

Building the research, and research leadership, capacity of research higher degree students and early career researchers working on cannabis medicines project.

Establishment of a ‘community of practice’ group to support capacity building of the next generation of researchers through a program of skills development and training; annual events; and strategic activities and initiatives to build capacity.

ACRE drives facilitation of Committee-led networking, co-mentoring and leadership development and collaborative opportunities and events for ACRE-based higher degree research students and early career researchers.

ACRE’s community of practice includes several postdoctoral fellows and early career researchers working on cannabis medicines projects, and five current PhD students, with more to commence post-COVID.

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Cannabis Medicines Prescribing Guidance

To support clinical decision making, and provide practical information to assist NSW-based medical practitioners in their the use of cannabis medicines within current Australian regulatory frameworks and clinical evidence.

- Anorexia Cachexia in Advanced Cancer
- Chemotherapy-Induced Nausea and Vomiting (CINV)
- Nausea in Palliative Care
- Dementia
- Non-Cancer Pain
- Spasticity

https://www.australiancannabinoidresearch.com.au/resources

National Guidance has been developed in collaboration with NPS https://www.nps.org.au/professionals/medicinal-cannabis-what-you-need-to-know

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Pharmacokinetic Laboratory Activities

Development of validated methods for analysis of plant material and patient samples

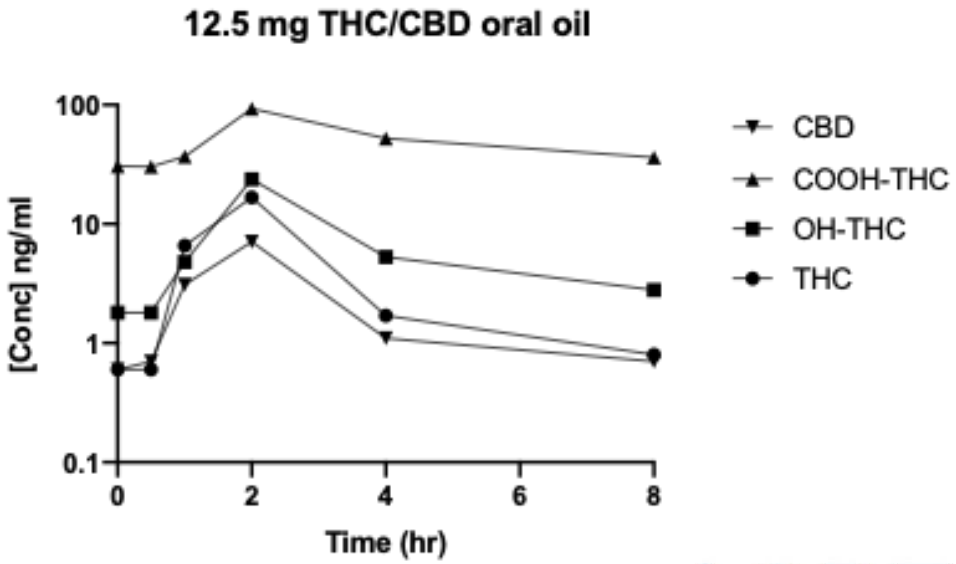
Validating storage and transport of patient samples, and stability of plant material and cannabis medicine

NSW Health Pathology collaboration

- NATA Accreditation
- Clinical cannabinoid blood analysis program

Currently available assays

- Plasma THC and CBD
- Cannabinoid profile (17 cannabinoids)



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CARE NSW

Cannabinoids for symptom control in Advanced cancer, an open label prospective clinical trial in NSW

The *CARE NSW Trial* is led by the NHMRC funded ***Australian Centre for Cannabinoid Clinical and Research Excellence (ACRE),*** and funded by the **NSW Government** through the ***NSW Clinical Cannabis Medicines Program***

CARE NSW Investigators

Professor Jennifer Martin	Chief Principal Investigator	**Associate Professor Peter Grimison**	Medical Oncologist (Metropolitan)	**Dr Peter Galettis**	Pharmacokinetic Scientist
Professor Meera Agar	Palliative Care Clinician	**Dr Rob Zielinski**	Medical Oncologist (Rural)	**Dr Zheng Liu**	Translational Researcher - Pharmacodynamics
Associate Professor Judith Lacey	Palliative Care Clinician	**Professor Kathy Eagar**	Research Psychologist	**Dr Catherine Lucas**	Clinical Pharmacologist and Nuclear Medicine Specialist
Professor Richard Chye	Palliative Care Clinician	**Dr Craig Dalton**	Public Health Clinician and Epidemiologist	**Associate Professor Jenny Schneider**	Pharmacist
Professor Nick Lintzeris	Addiction Medicine Clinician	**Professor Paul Scuffham**	Health Economist		

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CARE NSW Aim

To profile how advanced cancer patients use cannabis medicines in real-world via the collection of prospective data on the open-label product, dose, efficacy, safety, pharmacokinetics and pharmacodynamics; and

To provide preliminary safety, tolerability and efficacy evidence to guide future studies.

This study will also facilitate conditional free access to legal cannabis medicines for up to 600 advanced cancer patients across NSW.

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CARE NSW Trial Design

The CARE NSW Trial is a non-randomised open-label, Phase IV ‘real world’ clinical trial that includes a Phase II pharmacokinetic sampling component.

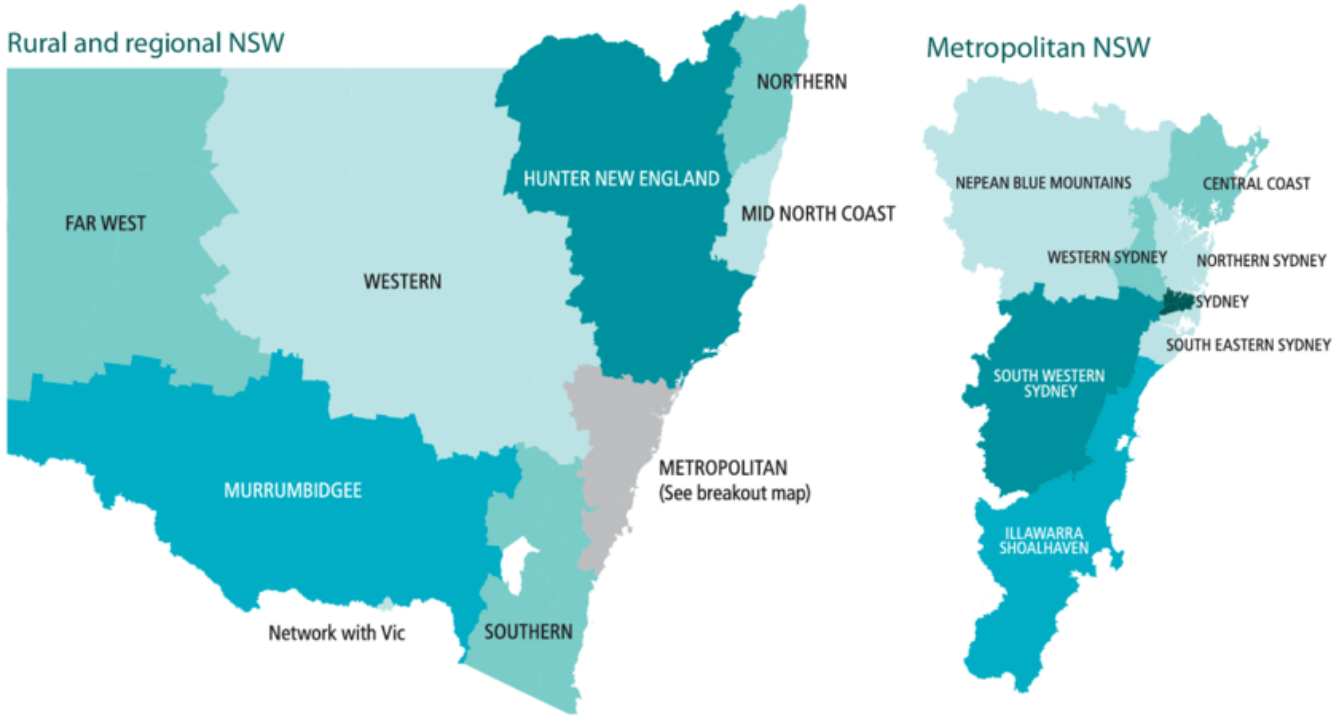
The trial is a preliminary study to describe the changes in a participant’s quality of life, clinical benefit, toxicity, tolerability and costs of a selection of cannabis medicines products available in NSW.

Health Condition: Advanced cancer with symptoms of anorexia, nausea, or refractory pain not responsive to current therapies

Sample Size: up to 600

Trial Duration: 3 years

CARE NSW is **approved** as a **NSW Cancer Institute Portfolio Level 3** (supportive of care)



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CARE NSW was designed to describe

- The **effect** a range of cannabis medicines have **on the 3 index symptoms** (nausea, anorexia, refractory pain), experienced by people with advanced cancer across NSW and the **side effects** of cannabis medicine in people with advanced cancer

- To understand what may be the best dose for symptom control in advanced cancer patients, by measuring blood levels of the cannabis medicines (**pharmacokinetics**) and relating them to a measurable outcome (pharmacodynamics)

- This study provides **compassionate long term access** - Until such time as patient withdraws, or is withdrawn (toxicity/ death)

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CARE NSW Objectives

Primary

- To **describe preliminary efficacy outcomes of cannabis medicines products on a range of key symptoms most relevant to patients with advanced cancer**, including index symptoms of pain, nausea, appetite as well as changes in other measures such as sleep, mood, and quality of life.
- To **characterise the preliminary pharmacokinetic** (Tmax, Cmax, bioavailability, AUC, T1/2) **and pharmacodynamic** (sedation, analgesia, side effects) **parameters of a number of cannabis medicines formulations** in a group of advanced cancer patients.
- To **determine the preliminary adverse effects and tolerance of cannabis medicines products** in an advanced cancer population including abuse liability and development of cannabis use disorder

Secondary

- To use the preliminary pharmacokinetic data collected, together with standard pharmacokinetic modelling tools, to **develop a population pharmacokinetic model of THC and CBD in an advanced cancer population**, including the factors contributing to inter- and intra-individual variability.
- To **examine the relationship between the product dose, pharmacokinetics of THC and CBD and efficacy and toxicity**.
- To **describe the change in concomitant medication use during the study.**
- To **examine the change in illicit cannabis use following access to a prescribed cannabis medicine.**
- To **identify the resource use and costs associated with cannabis medicines** in the advanced cancer population**.**
- To **develop a standardised set of safety and outcome measures to be used in future Australian clinical trials and clinical practice** use of cannabis medicines.

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CARE NSW Eligibility Criteria

Inclusion:

1. **Aged 18 years or older**
2. **Has provided written Informed Consent** for participation in this trial
3. **Confirmed advanced cancer (any)** with or without stable disease
4. **Predicted life expectancy of 6 to 12 months at the time of consent,** as estimated by the study investigator and confirmed by an additional qualified clinician, independent of the trial.
5. **Persistent symptoms of anorexia, nausea or refractory pain,** which in the investigator's opinion are not responsive to implementation of standard practice, and who are ineligible or not wishing to be involved in other clinical trials of cannabis medicines.
6. **Willing and able, in the investigator's opinion, to comply with all trial requirements**, including keeping a patient diary, completing clinical measurement scales and having pharmacokinetic samples collected as per Participant Information Sheet. Note: completion of these trial requirements is essential and intentional non-compliance may cease access to trial product and will be managed on a case-by-case basis. Non-compliance due to declining health is unintentional and it is hoped unintentional noncompliance due to declining health may be minimised through optional proxy completion of patient-reported outcomes and patient diary.
7. **Available to attend Trial Site for follow up and collection of investigational product.**
8. **Participants (and/or partners) capable of childbearing are using adequate contraception**

Exclusion:

1. **Lack of capacity to consent.**
2. **Unwilling to keep a Patient Diary, attend follow up appointments, complete clinical measurement scales or have pharmacokinetic samples**
3. **History of schizophrenia, other psychotic illness, severe borderline personality disorder, or other significant psychiatric disorder other than depression or anxiety associated with an underlying condition. Acute Delirium or a history of is also an exception.**
4. **Previous severe adverse event to any cannabinoid product, such as cannabis-related psychosis, panic attack, palpitations**
5. **A diagnosed substance use disorder** (ICD-10 criteria (abuse, dependence)) **to alcohol, opioids, cannabis, benzodiazepines, or illicit stimulants.** Nicotine and caffeine are excluded.
6. **Known allergy to cannabis or other ingredient of cannabis medicine e.g. carrier oil**

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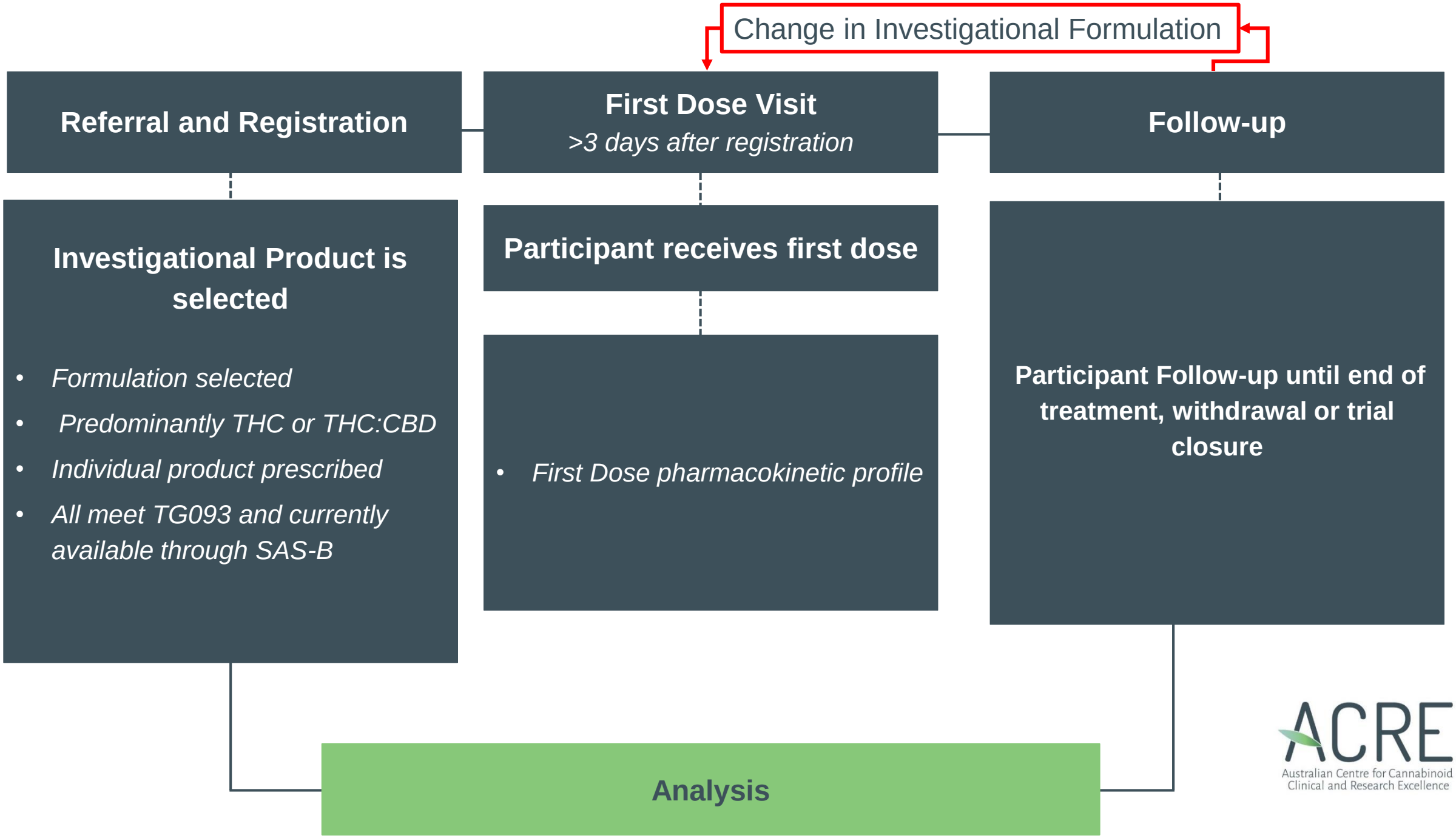

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CARE NSW Dosage Guidance

THC mg per dose (3x daily)	
1.25 mg	Minimum Dose
2.5 mg	Suggested Initial Starting dose Cannabis naïve participant
5 mg	Suggested Initial Starting dose in participant with previous experience of Cannabis
10 mg - 13.3 mg	*Case by case and by approval only*
>13.3 mg	*Exceptional Circumstances. Possible requirement to withdrawn from trial to access approval through an alternative pathway.*

Current guidance and existing practice is to:

- Start with a lower dose
- Titrate upwards to reach individualised dose where efficacy occurs with tolerable toxicity

A maximum tolerated dose for each drug daily will be set in line with TGA Guidance at 30 mg THC per day.

Participants who require a higher dose due to tolerance may be approved under exceptional circumstances to increase to a maximum dose of 40 mg THC per day, in line with current Queensland Health Guidance.

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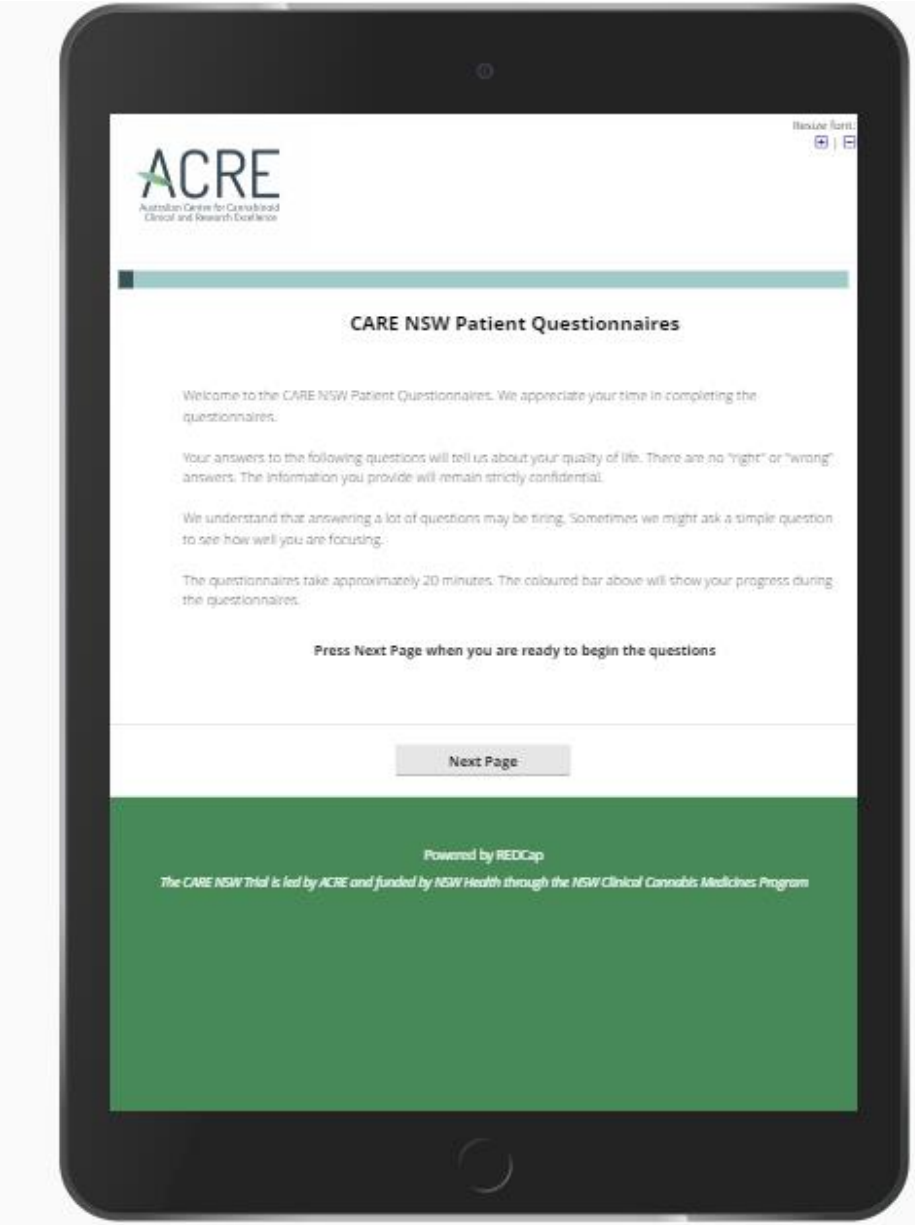
CARE NSW
Patient Reported Outcomes

Patient reported outcomes will be completed via a trial supplied iPad.

- EORTC QLQ-C30
- DASS-21
- TSQM
- PGIC
- Bespoke Modified ORBIT
- FAACT
- BPI



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CARE NSW Patient Diary

CARE NSW is utilising an online Patient Diary.

The Patient Diary is a mobile application that can be downloaded to the participants smart phone.

The Patient Diary will be completed:

- **daily for the first 6 weeks** and will then change to
- **once a week** until product is ceased

The diary consists of 3 sections:

- Symptom Assessment Scale (SAS)
- Medicinal Cannabis Tracker
- Breakthrough Medication Tracker

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CARE NSW Safety Reporting

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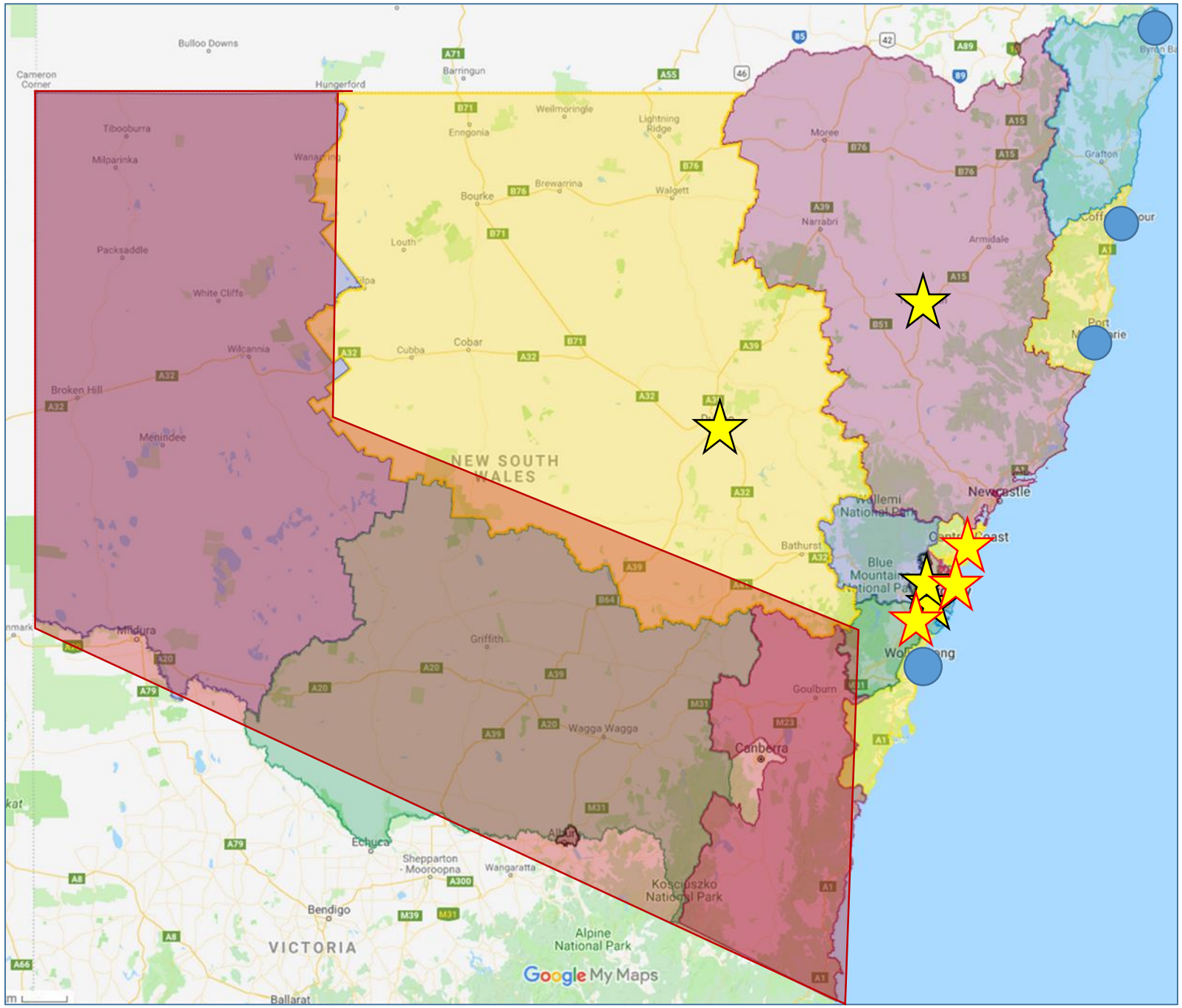
Reporting of adverse events and serious adverse events within the CARE NSW trial is in line with the 2016 NHMRC safety monitoring and reporting guidance

Adverse Events	The frequency, type, and severity of all non-serious adverse events will be recorded according to CTCAE v5.0 . This standard AE tool will be used to collect AE data on participants at every visit. The known side effects reported in the TGA Guidance of medicinal cannabis in palliative care will be targeted with the CTCAE.
Serious Adverse Events etc	Reporting of adverse events and serious adverse events within the CARE NSW trial is in line with the 2016 NHMRC safety monitoring and reporting guidance
	The DSMB will review individual reports and line listings of all SAEs, SUSAR and SSIs and a listing of all other AEs recorded at follow-up assessments via CTCAE v5.0 completion, quarterly to guide its assessment of whether the trial should be stopped or undergo modification or continue without change.



CARE NSW Sites

1. Orange Health Service
2. Chris O'Brien Lifehouse
3. Liverpool Hospital
4. Tamworth Hospital
5 and 6. Gosford/Wyong Hospitals
7. Prince of Wales Hospital
8. Westmead Hospital

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The Data analysis timeline in CARE NSW

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Interim Pharmacokinetic Analysis	Per product and first dose, after 10 participants on an individual product at the same first dose
Safety Analysis	Quarterly
Interim Analysis	If and as directed by Data Safety and Monitoring Board
Main Analysis	3 years 6 weeks
Final Analysis	All participants off trial

Why we CARE

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CARE NSW Trial will …

- Be the largest investigator led medicinal cannabis trial, and first of its kind, enabling NSW to lead the world in clinical research into the safe use of cannabis medicines

- Enable the provision of monitored legal access to pharmaceutical cannabis medicines for a significant advanced cancer population, including patients in regional and remote areas in NSW, at no cost.

- Strengthen the internal evidence-base on cannabis medicines to enable timely translation into clinical practice

- Direct the Australian-focus on medicinal cannabis research, improve consumer knowledge, and provide GPs with prescriber confidence

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CARE NSW Trial Further Information

ANZCTR
http://www.ANZCTR.org.au/ACTRN12619000265178p.aspx

ACRE
https://www.australiancannabinoidresearch.com.au/clinical-trials

NSW Health
https://www.medicinalcannabis.nsw.gov.au/health-professionals/clinical-trials/advanced-cancer

ClinTrailRefApp
https://web.clintrialreferapp.com/SearchTrial/Details?trialId=S3LnImfWKwE%3D

Social Media Participant EOI (if approved by Ethics)

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THANK YOU

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