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Cannabidiol as an Adjunct for the Treatment of Anorexia Nervosa (CAFTAN): An Open Label Pilot Trial with Extension in Young People

Medical Clearance Form

Date:

Dear _____ [*GP name*],

RE: [*Participant name]*

Ms/Mr [*Participant name]*, has advised us that you are her/his/their treating medical practitioner (general practitioner or pediatrician). He/she has agreed to participate in an open-label trial conducted by the University of Sydney for cannabidiol (CBD) treatment for anorexia nervosa as an adjunctive intervention alongside Maudsley Family-Based Treatment (MFBT) he/she is receiving as part of routine clinical care in the community for anorexia nervosa. You may be aware that MFBT delivered in the community is the first line evidence-based treatment for anorexia nervosa in children and adolescents, however the refeeding phases of treatment are anxiety-provoking for the young person. This study examines whether anxiety can be reduced by adjunctive CBD treatment. CBD has recently been shown to be safe in young people and highly effective in managing treatment-resistant anxiety. As you know, medical practitioners play a very important role for patients and their families undergoing treatment for anorexia nervosa, and as such we would like to provide you with information about the trial and ask for your help in collecting important data.

To confirm the young person's eligibility for the trial, they require a complete medical assessment confirming they are medically stable. As you may be aware, anorexia nervosa comes with a risk of medical complications and, at times, instability. As such, medical clearance and regular monitoring is required even during therapy aimed at weight restoration like MFBT. We would be grateful if you would agree to be involved by providing medical support and monitoring for the duration of the trial.

The trial will start from [date] and end on [date](at the latest), unless we advise you that this period has been extended.

If you agree to be involved, you must acknowledge that:

- You consent to be the participant's nominated medical practitioner for the duration of the study,
- You have medically checked the participant and will share the test results with the research team,
- Confirm that they are medically stable,
- Will hold responsibility for medical assessment and escalation (when required),
- Will continue to medically monitor the participant, weekly recommended for the first month then at intervals deemed most appropriate by you,
- Will conduct weekly liver function tests for the first month then monthly for the duration of the study and to share these results with the research team,
- Will agree to a phone call with the trial doctor to review suitability and establish communication pathways prior to initiating the trial medication
- Will be available to speak to the trial doctor for the duration of the study.

We would be grateful if you could share a copy of the ED Plan used to refer this patient to the MFBT practitioner. To ensure that the data included is complete, please refer to this document – GP Quick Tools – for more information or access to a template form.

In addition, we ask specifically if you could complete the following:

- A urine test to confirm absence of illicit drugs,
- A urine test (if female) confirming they are not pregnant,
- A discussion with the participant about effective and reliable use of contraception during the trial, with or without the presence of parents where appropriate. It is important that the participant does not fall pregnant (or impregnate a sexual partner if male participant) while taking the investigational drug. This will be reiterated to the participant as they enter the trial by the research staff.

Clinical responsibility for management of the patient remains, at all times, with the treating team in the community (i.e., you, medical practitioner and the therapist) as per usual practice. Please let the research staff know if at any time you believe the participant's medical status changes otherwise or if you believe that they may no longer be suitable for the trial.

The research team will notify you if there is any evidence of rapid weight loss for the participant (as per the trial criteria) or other indicators that the parent/participant shares with the research team that could potentially change their medical status. In this case, you will be contacted by the research staff and asked to monitor the participant's medical parameters. If you have any concerns or questions at any time, you can reach out and discuss with trial doctor or research team.

As per usual practice, the therapist will be in communication with you.

We are very interested in the perception of health professionals of new treatments, so you will also be asked to complete a brief survey at the end of the trial to share your thoughts on the efficacy of CBD as an adjunct to MFBT.

An appendix has been included detailing further information about the trial and guidelines for how to monitor the participant through the trial.

For support from your local Eating Disorder Coordinator, such as to discuss local service pathways, treatment providers and training opportunities, please visit: https://www.slhd.nsw.gov.au/mentalhealth/pdf/NSW_Eating_Disorder_Coordinators.pdf

If you have any questions, please contact myself, trial specialist GP [Karen Spielman via the trial email], or the research staff at the University using the contact details provided below.

I _____ [*medical practitioner name*] agree that patient [*participant name; DOB*] is safe to participate in the trial.

I can confirm that:

1. I have medically checked the patient
2. I agree that he/she is medically stable to participate in the trial with the interventional drug, cannabidiol.
3. I understand that I must medically monitor the participant as frequently as clinically indicated (weekly for the first month)
4. I understand that I hold responsibility for the medical assessment and escalation (if required) of the young person
5. I consent to be the participant's nominated medical practitioner for the duration of the study.
6. I understand that in addition to urgent communication, I will receive regular written correspondence from the treating clinicians updating me on the young person's treatment progress.

Name: _____

Provider Number : _____

Phone : _____

Email : _____

Signature : _____

Date : _____

Your Sincerely,
Sarah-Catherine Rodan
University of Sydney
Phone: 0403224986
Email: sarah-catherine.rodan@sydney.edu.au

Please note: Contact hours for the University of Sydney are Monday to Friday, 9 a.m. to 5 p.m 0456 783 739. In the case of a psychiatric emergency please contact the Mental Health Line on 1800 011 511. If you require urgent medical assistance please call 000 or refer the participant to the local emergency department

Appendix A

Information for Medical Monitoring of Patients

As part of the study, and for ethical and safety considerations, the participants are asked to have a general medical check-up to ensure their current medical stability. As per the ED plan we advise a general medical examination with specific attention to weight (body mass index), ECG, pulse, blood pressure, and blood tests as per attached guidelines, random blood sugar, electrolytes (especially potassium and phosphate, also zinc and magnesium levels), renal function, liver function, albumin, haematology and baseline thyroid function, and iron status, B_{12} and folate.

We also ask you to discuss if there are any risks of pregnancy with the patient without the presence of parents and to order a urine screen to check for illicit drug use and pregnancy. If you are unsure regarding participant's risk of pregnancy please contact the trial doctor to discuss.

Thank you for assessing and taking medical care of the person throughout the trial and community treatment.

Monitoring Medical Signs

If the young person reports symptoms of possible medical instability, they must see their medical practitioner immediately. If the young person cannot see their medical practitioner, they are *advised to* present to their nearest Emergency Department for an assessment. Possible symptoms could include:

- Feeling like fainting or passing out when going from sitting to standing
- Constipation
- Nausea
- Shakiness
- Headaches
- Weakness

If the young person describes or the family reports the young person experiencing any of the following symptoms, they are *required to* present to their nearest Emergency Department or call 000 immediately:

- Shortness of breath
- Chest pains
- Rapid or low heart rate
- Fainting
- Dizziness
- Loss of consciousness
- Confusion
- Weakness
- Oedema/ swollen ankles
- Palpitations
- Vomiting of blood
- Abdominal distension
- Abdominal pain
- Muscle pain
- Tingling around mouth and/or fingers and toes

Monitoring Liver Function

Elevated liver serum enzymes are common in anorexia nervosa, due to malnutrition and/ or re-feeding. While elevated liver function enzymes have not been reported in trials investigating CBD outside of paediatric epilepsy in young persons, this has been reported in healthy adults. It is imperative that liver serum enzymes are monitored **weekly** for the **first month** of the trial and then **monthly for the duration of the study**.

Weight Loss Management Plan

Given the risks associated with weight loss, the following weight loss management strategy will be used for all participants.

As is for routine MFBT the weight and BMI will be measured at each session by the MFBT clinician. Weight will be taken as per the treatment manual, at the same time of day and on the **same scales**, with the young person wearing light clothing and after the bladder has been voided. The clinician will inform the research team of the weight on a weekly basis. The research team will communicate with you if the patient has rapid weight loss at any point during the trial.

If your patient is attending MFBT via telehealth there will need to be the opportunity either for parents to weigh or for the medical practitioner to take over this role. The clinician will work this out with the family, so each family can be engaged around what will work. **The same scales will need to be used for the duration of the trial and the research team informed of the weight weekly.**

Response to Rapid Weight Loss:
If there is evidence of rapid or consistent weight loss*, the following actions are put in place:

- The study coordinator is alerted by the community clinician, and,
- The participant's nominated medical practitioner is notified via email, and the participant is recommended to see their medical practitioner for medical assessment
- The participant will be discontinued from the trial if there is any observable deterioration in participant's medical or psychiatric parameters as noted by medical practitioner, therapist or above indicators. In this instance, the discontinuation protocol would be activated. The therapist and/or study coordinator would advise the participant, their family and their medical practitioner verbally and in writing that they were discontinued from the study.

*Rapid weight loss is indexed by > 1kg a week for two weeks. Note that this is different definition to the NSW Eating Disorders Toolkit (2018). This ensures that the IOI site holds a lower risk threshold.

If you observe any of the following at anytime please ensure the patient has assessment at an emergency department as needed. Further, if the below indicators are reported by the young person, family or medical practitioner to the therapist, the therapist will encourage the family to attend their local hospital for an urgent assessment:

Indications for Hospitalisation

A hospital admission may be indicated for any of the following criteria:

- Heart Rate <50 bpm,
- Cardia arrhythmia including a prolonged QTc interval (>450 msec)
- Postural tachycardia >20bpm increase heart rate
- Blood pressure <80/40 mm/Hg or postural drop >30 mm/Hg
- Temperature < 35.5°C
- Low serum potassium ≤3.0 mmol/L
- BSL <3.0mmol/L
- Other significant electrolyte imbalances
- BMI ≤ 14
- Rapid or consistent weight loss (e.g., > 1kg each week for six or more weeks)
- Acute dehydration or patient has ceased fluid intake
- Intensive community-based treatment has proven ineffective
- Comorbid or pre-existing psychiatric conditions that require hospitalisation
- Suicidality with an active intent and plan
- Other special considerations such as diabetes or pregnancy

Figure 1. Indications for hospitalisation according to the NSW Eating Disorders Toolkit (2018)

As is routine for MFBT treatment we advise that participants attend ongoing medical monitoring appointments with you for the duration of the trial at intervals you determine for adequate medical monitoring or otherwise.

It is not anticipated that there should be any serious side effects from this treatment. However, if you become concerned regarding the participant's medical stability throughout the trial or consider him/her to be unsafe to participate in the trial, please notify us and refer the participant for additional care appropriately according to the National Eating Disorder Collaboration's Professional Resource for General Practitioners. You can access the guidelines using the following link: https://insideoutinstitute.org.au/resource-library/eating-disorders-a-professional-resource-for-general-practitioners. Additionally, if you are unsure about how to detect and respond to high-risk symptoms or behaviours please refer to the guide created by the Victorian Centre of Excellence in Eating Disorders (CEED) titled, 'Physical Risk in Suspected Eating Disorders Mental Health Clinician Response Guide', which can be accessed using the following link. http://www.ceed.org.au/sites/default/files/resources/documents/CEED_Handout_ED%20Physical%20Risk%20Management%20-%20Mental%20Health%20Clinician%20Response%20Guide_May2017_ES_Colour.pdf.

You may also contact the trial GP specialist for guidance.

Appendix B – Parent Information Sheet

Cannabidiol as an Adjunct for the Treatment of Anorexia Nervosa (CAFTAN): An Open Label Pilot Trial with Extension in Young People

Information Sheet – Parent

(1) Introduction

This is an invitation for your child to take part in a research project testing a new treatment for anorexia nervosa. The young person has been invited to take part because they have anorexia nervosa, are aged between 12-18 years old, are about to commence Maudsley Family-Based Treatment in the community and are in the care of a medical practitioner (GP or paediatrician).

This Information Sheet provides you with information about the research project. It explains the treatments involved and what will be required of you and your child if you choose to participate. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. If you have any questions or would like more information, you can speak to the trial coordinator, Sarah-Catherine Rodan, on **+61403224986**. Feel free to discuss the information in this sheet with a relative, friend or your child's medical practitioner before making your decision.

Participation in this research is voluntary. If you do not wish your child to take part, they do not have to. This will not impact the quality of their care or access to care in any way.

The research is being sponsored by the University of Sydney and conducted by the Lambert Initiative for Cannabinoid Therapeutics and the InsideOut Institute for Eating Disorders. The results of this research will be used by the study investigator Sarah-Catherine Rodan to obtain a doctorate (PhD) degree.

If you decide you would like your child to take part in the research project, you will be asked to sign a consent form, which you will find at the end of this Participant Information Sheet (and which is yours to keep).

(2) What is the purpose of this research?

This study aims to determine the safety and effectiveness of a new pharmacological treatment, cannabidiol (CBD) – the non-intoxicating component of the cannabis plant – that has been demonstrated to be effective

for treatment of anxiety in young people (12-25 years old). This study will pilot this treatment in young people with anorexia nervosa who are about to commence Maudsley Family-Based Treatment (MFBT).

Anorexia nervosa is often characterised by high levels of anxiety, particularly in the early stages of treatment where refeeding and weight gain is needed. Anorexia nervosa also frequently co-exists with other anxiety disorders. We hypothesize that by targeting the anxiety with this medication we may be able to make therapy easier to deliver, better tolerated by the young person, easier for parents and carers to manage and, ultimately, improve recovery rates.

MFBT is the most evidence-based treatment for anorexia nervosa in young people. However, many individuals do not recover. Ongoing clinical research has been looking for ways to improve MFBT to enhance outcomes for young people. High anxiety around food, weight, and body shape are central features for all young people with anorexia nervosa. MFBT can increase these anxieties because early stages of treatment require the child / young person to be re-fed and gain weight. In order to recover, they typically need to eat large quantities of food and gain significant amounts of weight.

In the early stages of treatment, parents are put in charge of the roles of refeeding and weight gain and supported by the MFBT therapist to do this. Eating disorder-driven resistance to re-feeding and weight gain is often a result of the extreme anxiety the young person is experiencing and can make these tasks more challenging for parents. Therefore, an intervention that aims to reduce this anxiety **may make treatment easier to deliver, reduce the stress on families and the young person and improve response to MFBT, subsequently improving weight gain and eating disorder recovery.**

Your child's participation in this study will benefit the eating disorder research community and may benefit your child as well as future patients by helping us to develop, implement and improve current treatment programs for problematic eating behaviours and long-term recovery.

We cannot guarantee that your child will receive benefit from this trial however, we have new evidence of the effectiveness of CBD from a study we completed in young people aged 12-25 with severe treatment-resistant anxiety, who had not responded to other medication/therapies. CBD was administered over 12 weeks with the same dose in this study (800 mg/day) which produced a higher than anticipated reduction in anxiety. Two-thirds of participants had a >33% reduction and 40% of participants had a >50% reduction in anxiety by end of treatment. Please refer to the Lambert Initiative website for further details about this

study (https://www.sydney.edu.au/lambert/our-research/anxiety.html). This provides a strong incentive to explore this treatment in young people with anorexia nervosa.

(3) What is CBD?

The new treatment, cannabidiol (CBD), is a non-intoxicating compound known as a 'cannabinoid' extracted from the cannabis plant. The cannabis plant contains hundreds of different cannabinoids with the two most studied being cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). Unlike THC, CBD is non-intoxicating and will not get your child 'high' or 'stoned'. CBD will be administered in the form of a capsule.

CBD is widely prescribed in Australia to treat a variety of conditions including anxiety, chronic pain (including cancer pain and symptoms), epilepsy, and insomnia. CBD is known to have a good safety profile and side effects are typically mild and tolerable.

Cannabidiol (CBD) is considered an experimental drug and has not been approved in Australia for the treatment of anorexia nervosa. This study will be conducted under the Therapeutic Goods Administration (TGA) Clinical Trials Notification (CTN) Scheme and has been approved by a Human Research Ethics Committee (HREC). This allows the investigators to use this product for medical research purposes.

(4) What does the young person's participation in this research involve?

(4.1) Maudsley Family-Based Treatment (MFBT)

You and your child will attend MFBT with the clinician you have engaged with. MFBT is an evidence-based three-stage treatment program that supports parents to manage weight restoration and curtail eating disorder behaviours in their children in an attempt to achieve recovery. It is the first line treatment for young people with anorexia nervosa in this age group because at this stage it is the only one with sufficient research supporting its efficacy.

Your child's weight will be monitored at every session as a standard measure of your child's progress. Your clinician will weigh your child on the **same set of scales**, and around a similar time of day where possible. The same scales must be used for the duration of the study. Your child will be weighed clothed, but will be asked to remove their jumper and shoes, and to void their bladder prior to weigh-ins. Your child's weight will be shared with other members of the treating team.

If you are attending treatment via telehealth, your clinician will discuss with you the best way to undertake the weekly weigh-in. This may include asking the family to complete the weigh-in or for the medical practitioner to take over this role. The clinician will work this out together with the family.

(4.2) CBD investigational drug

Your child will be prescribed CBD capsules. As the parent, you will be responsible for administering CBD to your child. You will be sent the medication via post to the address you provide free of charge. The treatment with CBD will begin at the commencement of MFBT and will continue every day for 12 weeks.

In certain circumstances, your child may have the opportunity to continue taking CBD until the end of MFBT (week 24) as part of the trial. Your child will continue the same dose of 800 mg/day and will continue completing monthly questionnaires. If your child would like to continue taking CBD, and you consent to this, your treating team will assess whether this is appropriate.

Dosing will start at:

- Week 1: 200 mg/day (1 capsule at night)
- Week 2: 400 mg/day (1 capsule in the morning + 1 capsule at night).
- Week 3: 600mg/day (1 capsule in the morning + 2 capsules at night).
- Week 4-Week 12: 800mg/day (2 capsules in the morning + 2 capsules at night).

- Extension arm: Week 12-Week 24: 800mg/day (2 capsules in the morning + 2 capsules at night).

You will be provided with a medication card with clear dosing instructions and contact details of the trial coordinator and trial doctor. If a dose is missed, you will need to give the missed dose as soon as possible and inform the trial doctor immediately.

Throughout the trial you **must keep all the bottles (including any unused CBD capsules)**. After the trial has concluded you must return the bottles (including any unused CBD capsules) to the research team. We will organise a courier to collect this.

Please be aware that further access to CBD will not be made available to you after this trial has been concluded.

(4.3) Medical Management with your Medical Practitioner

Regular medical review is an important component of treatment for anorexia nervosa. To ensure the safety of your child , it is a requirement of this trial that your child is monitored regularly by their medical practitioner throughout the duration of the trial.

Upon entering the trial, your medical practitioner will be given a form to complete. Information from your child's medical records will be collected as part of clinical care during the intake assessment and referral process. The medical practitioner is then asked to confirm that your child is medically stable, not pregnant (if applicable) and that there has been no use of illicit drugs in the past 4 weeks, as confirmed with urine test. Your medical practitioner will be required to inform the research staff if there is any deterioration in your child's medical or mental health as this may impact their eligibility to continue taking the CBD. This information will be kept strictly confidential. **The safety of your child is our priority.**

(4.4) Trial doctor

The trial doctor will complete telehealth sessions with you and your child at intervals specified at their discretion and a phone call prior to each dose increase (start of Week 2, 3 and 4). This is in addition to the routine medical review, as above, with the medical practitioner.

(4.5) Questionnaires, assessments, and forms

In agreeing to participate in the trial, your child will be required to complete a series of questionnaires which will gather information about their eating disorder symptoms, anxiety levels, and general mental health. The parent will also be required to complete one questionnaire throughout the trial.

If your child is aged 12-15 years, you will be sent a link via email for your child to complete online. If your child is aged 16-18 years, an email will be sent to them directly to complete. Email reminders will be sent to you / your child as needed. Each questionnaire will take between 5-25 minutes to complete. The questionnaires will include the following:

- *Eating Disorder Examination Questionnaire (EDE-Q):* A 28-item questionnaire to measure eating disorder symptoms.
- *Yale-Brown-Cornell Eating Disorder Scale Self Report Questionnaire (YBC-EDS-SRQ):* A 19-tem questionnaire to measure obsessive and compulsive symptoms.
- *Overall Anxiety Severity and Impairment Scale (OASIS)*: A 5-item questionnaire to measure anxiety symptoms.
- *Beck Depression Inventory (BDI-II):* A 21-item questionnaire to measure depression.
- *Quality of life (EQ-5D-Y or EQ-5D-5L*): A 6-item questionnaire to assess quality of life.
- *Child-Adolescent Perfectionism Scale*: A 22-item questionnaire to measure perfectionism
- *OASIS-Youth*: A 7-item care-giver report of the young person's anxiety **(completed by the parent).**

The questionnaires will be administered at baseline, end of Week 4, Week 8, and Week 12 (a total of 4 times).

If your child continues treatment (as part of the extension arm), the questionnaires will continue to be administered at the following intervals: end of Week 16, Week, 20, and Week 24 (end of treatment) and at three-month follow-up (a total of 8 times).

Once the trial has been concluded, you will be invited to complete a short survey to share your experience with the CBD treatment. As mentioned previously, weight and height will be measured routinely throughout the treatment by your child's treating MFBT clinician (or via alternative arrangement if you are using telehealth treatment) and medical practitioner. Your medical practitioner will be required to confirm the weight and height of your child at three-month follow-up.

(4.6) Urine Samples

Collection of urine is a mandatory component of the research. Prior to the commencement of the study, a urine sample will be collected by the medical practitioner from your child to confirm absence of illicit drugs.

You will also be asked to collect a sample of urine every month using specimen containers provided to you at the start of the trial. We will organise for a courier to collect the urine sample from your home address and ship it to our laboratory at the Brain and Mind Centre at the University of Sydney. **Please store the urine sample in the fridge until the courier arrives to pick it up.** The urine sample will be analysed for CBD to ensure medication adherence.

(5) What does the parent have to do?

As the parent you will be required to ensure the CBD treatment is taken regularly in accordance with the instructions provided. You will be responsible for handling the study medication and dispensing it daily to your child. If a dose is missed, you will need to administer the missed dose and inform the trial doctor immediately. You will also need to commit to attending all MFBT sessions and ensuring that your child is seen regularly by your medical practitioner.

(6) Other relevant information about the research project

This is a small open-label trial. We aim to recruit 30 participants in the community. 'Open label' means that everyone will be receiving the same treatment and will know which treatment they are receiving.

(7) Does your child have to take part in this research project?

Participation in any research project is entirely voluntary. If you do not wish for your child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw them from the project at any stage.

Your decision to take part or to withdraw from the trial **will not affect** your child's treatment or you/your child's relationship with their treatment team, or with the researchers at the University of Sydney, Lambert Initiative for Cannabinoid Therapeutics, or InsideOut Institute for Eating Disorders.

(8) What are the alternatives to participation?

Your child does not have to take part in this research project to receive treatment. Other options are available; these include continuing with MFBT treatment as usual with no drug intervention. You can also discuss other treatment options with your child's medical practitioner.

(9) What are the possible benefits of taking part?

We cannot guarantee or promise that your child will receive any benefits from this research. This study will contribute to important research into the effects of CBD treatment on anorexia nervosa. This evidence may assist in improving pharmacological treatment for eating disorders in the future, even if this does not benefit you and your child directly.

(10) What are the possible risks of taking part?

(10.1) Cannabidiol

Overall, CBD is generally well-tolerated and has a good safety profile. It is non-intoxicating and does not cause addiction, dependence, or tolerance. The most common side effects include nausea, headaches, gastrointestinal upset and sometimes changes to liver function (raised liver enzymes) which may be accompanied by symptoms below:

Tell the study doctor if you notice any of the following side effects:

- Nausea, vomiting and/or diarrhea
- Fever or feeling unwell
- Unusual tiredness or sleepiness
- Pain or discomfort in the right upper stomach area
- Chest pain

Other side effects observed in a recent 12-week trial of 800mg/day CBD treatment in young people with treatment-resistant anxiety included fatigue, low mood, insomnia, changes in appetite, headache, and gastrointestinal upset. Side effects were mild-to-moderate in severity and transient (resolved).

Medical treatments often cause side effects. Your child may have none, some or all of the effects listed above, and they may be mild, moderate or (very rarely) severe. If your child has any of these side effects, **please contact the trial doctor immediately**. Their contact details will be listed on the medication card given to you.

Note that changes to liver function are common in anorexia nervosa. This may be due to malnutrition and/or re-feeding. To closely monitor your child's liver function, your medical practitioner will **conduct blood tests weekly for the first month** and then **monthly for the rest of the study duration**.

The effects of CBD on the liver can be exacerbated by the use of other medications. This is known as a 'drug-drug interaction'. **It is important that you inform your medical practitioner and trial doctor of the use of any new medications (prescription, over-the-counter, complementary and supplements) throughout your child's participation in the trial.** Should any signs of potential drug-drug interactions develop, the trial doctor and GP will review their treatment plan and may discontinue the drug intervention but continue with MFBT.

There may be other side effects that the researchers do not expect or do not know about, and that may be serious. Please note that this would be highly unlikely. You should tell the trial doctor **immediately** about any new or unusual symptoms. Most side effects are temporary and go away shortly after treatment ends.

(10.2) Pregnancy and risks to unborn child

It is important that your child is not pregnant and does not become pregnant (or impregnate a sexual partner if male) during the course of the trial. The young person will not be eligible to participate in the trial if pregnant or trying to become pregnant. This will be confirmed by the medical practitioner using a urinary pregnancy test.

If your child is female and of child-bearing potential (i.e., menstruating), the medical practitioner will discuss appropriate and reliable contraception if deemed appropriate (e.g., oral contraceptive, or long-acting reversible contraception such as a hormonal implant, injection, or IUD). Anorexia nervosa can cause amenorrhea (the absence of menstruation); however, ovulation can still occur without menstruation. Therefore if your child is sexually active, they must use appropriate contraception.

If your child is male, they are strongly advised to use effective contraception (e.g., condoms) and to not donate sperm during the course of the trial and for at least 7 days after the last dose of study medication. The medical practitioner will provide sexual health counselling to support their participation in the trial.

If at any time you think your child (or your child's sexual partner, if male) may have become pregnant, it is important to let the trial doctor know immediately.

(11) What will happen to my child's urine samples?

Urine samples will be stored at the Brain and Mind Centre Freezer Bank at the University of Sydney, Camperdown until analysis is completed to check for medication adherence. Any remaining samples will be destroyed after analysis.

(12) What if new information arises during this research project?

Sometimes during a research project, new information becomes available about the treatment that is being studied. If this happens, the trial doctor will tell you about it and discuss with you whether you want your child to continue in the research project. If you decide to withdraw your child from the study, they will continue with their other treatment as usual.

(13) Can the child have other medicines during this research project?

No, you must notify the researchers of any planned changes to current medications or procedures while your child is participating in this study.

You must tell us about any medicines your child may be using. This is in your child's interest as well as being important for the study because they may interact or interfere with the study drug. You must tell us about any prescription (antidepressants or mood stabilisers) or over-the-counter medications, including vitamins, herbal remedies, or other supplements your child is taking.

You should also tell the trial doctor about any changes to these during the young person's participation in the research project. The trial doctor will explain to you, which treatments or medications need to be stopped for the time the child is involved in the research project.

(14) What if I withdraw the child from this research project?

If you decide to withdraw your child from the project, please notify the trial doctor or a member of the research team before you cease taking the CBD medication. This notice will allow the trial doctor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your child during the research project, the trial doctor and relevant study staff will ask if you and your child if you are willing to complete a brief exit questionnaire (XX mins to complete) and will ask about reasons for withdrawing.

Following this, no further personal information will be collected. Personal information already collected will be retained to ensure that the results of the research project can be measured properly. You should be aware that data collected up to the time of withdrawal will form part of the research project results. If you do not want this to happen, you must inform a member of the research team before the participant enrols in the research project.

(15) Could this research project be stopped unexpectedly?

This research project may be changed or stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects in multiple participants or
- If the trial doctor decides it is in the best interest of your health and welfare to stop.

(16) Are there any reimbursements?

The cost of the medication and medical oversight by the trial doctor will be provided free of charge. This does not include costs associated with visits to your child's medical practitioner (i.e., GP or paediatrician) or any tests order by your medical practitioner. The cost of the MFBT sessions will not be covered, however, a rebate is available with the ED plan. There are no additional costs associated with participating in this research project. No additional reimbursements will be provided to you or child for your participation in the research project.

(17) What happens when the research project ends?

You will receive (via email) a summary of the major research findings once the trial has concluded and data analysis activities are complete. The results of this research will also be used for manuscript preparation and submission for publication as well as presentation to conferences. No participants will be identified in any report or publication of this study or its results.

We will share the study results by publishing them in relevant journal articles and / or presenting them at national and international scientific conferences. We will make sure that information is published /presented in such a way that neither you nor your child are identifiable.

Your child's data will be securely stored for a minimum of 15 years after the study finishes or until the youngest participant turns 25 years.

(18) What will happen to information about your child?

By signing the consent form you consent to the trial doctor and relevant research staff collecting and using personal information about your child for the research project. Any information obtained in connection with this research project that can identify your child will remain confidential and secure, except when:

- It is subpoenaed by a court,
- Failure to disclose information would in the reasonable belief of the clinicians place you, your child or another person at serious risk,
- Your prior approval has been obtained to discuss material with another person (e.g., a parent, employer or health provider). It is a requirement of participating in this study that your therapist can regularly communicate with your GP.

All data and participant information collected for the purposes of this study will be entered electronically and stored on a research database named REDCap (Research Electronic Data Capture). This is a secure, web-based, non-commercial, data management tool designed for research purposes, hosted, and backed up on the University of Sydney servers on a daily basis. The data will be analysed by the researchers at the University of Sydney. Your child will be identified with a unique participant code, assigned at enrolment. The key linking your child with their unique trial code will be stored in a password encrypted file, accessible only to the research staff. Your child will not be identified in any report or publication of this study or its results.

Information about participation in this research project may be recorded in your child's health records when they visit their local GP only with your permission.

In accordance with relevant Australian NSW privacy and other relevant laws, you have the right to request access to the young person's information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your child's information.

(19) Complaints and Compensation

If the participant suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging

appropriate medical treatment for the participant. If the participant is eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

In addition, you may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available the participant's injury or complication is sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). You and the participant do not give up any legal rights to compensation by participating in this study.

Research involving Humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the Sydney Local Health District – RPAH Zone (Protocol No. X21-0440). As part of this process, we have agreed to carry out the study according to the National Statement on Ethical Conduct in Human Research (2007). If you have any complaints about the ethical nature of this research project, please contact the Sydney Local Health District using the details outlined below. Please quote the study title and protocol number.

- **Telephone:** (02) 9515 7035
- **Email:** SLHD-RPAEthics@health.nsw.gov.au

(20) Who is organising and funding the research?

The research is being organised and funded by the InsideOut Institute for Eating Disorders and Lambert Initiative for Cannabinoid Therapeutics from the University of Sydney.

(21) Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Sydney Local Health District.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

(22) Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project you can contact any of the following people:

Clinical contact person:

Name	Sarah-Catherine Rodan
Telephone	0403224986
Email	sarah-catherine.rodan@sydney.edu.au

For matters relating to the interventional drug, the CBD capsules:

Trial doctor:

Name	Dr Karen Spielman
Email	drkarenspielman@gmail.com

Appendix C
List of Investigators

Principal Investigator (Trial Oversight)

Name:	Professor Iain McGregor
Address:	Brain and Mind Centre, 94 Mallet Street, Camperdown NSW 2050
Telephone:	+61 2 9351 3571
Email:	iain.mcgregor@sydney.edu.au

Principal Clinical Investigator (Medical/Supervision of Trial doctor)

Name:	Professor Janice Russell
Address:	RPAH, Marie Bashir Centre, 67-73 Missenden Rd, Camperdown NSW 2050
Telephone:	+61 2 9515 1430
Email:	janice.russell@sydney.edu.au

Co-investigator (Trial doctor/GP specialist)

Name:	Dr. Karen Spielman
Address:	InsideOut Institute for Eating Disorders, Charles Perkin Centre (D17), Camperdown NSW 2006
Email:	karen.spielman@sydney.edu.au

Co-investigator (Trial Oversight)

Name:	Dr. Sarah Maguire
Address:	InsideOut Institute for Eating Disorders, Charles Perkin Centre (D17), Camperdown NSW 2006
Telephone:	+61 2 86271910
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Co-investigator (Clinical trial coordinator/PhD Student)

Name:	Ms Sarah-Catherine Rodan
Address:	Brain and Mind Centre, 94 Mallet Street, Camperdown NSW 2050
Telephone:	+61 4 XXXXXXXX
Email:	sarah-catherine.rodan@sydney.edu.au

Co-investigator (Trial management)

Name:	Dr. Jane Miskovich-Wheatley
Address:	InsideOut Institute for Eating Disorders, Charles Perkin Centre (D17), Camperdown NSW 2006
Telephone:	+61 4 1336668

Email: Jane.miskovic-wheatley@sydney.edu.au