ENDEAVOUR
College of
Natural Health

Participant Information Sheet

Protocol Number	ANZCTRN: 12618000288224
Study Title	A Phase 2 placebo-controlled, double-blind randomised clinical trial assessing the efficacy of a Herbal supplement for Noctural enuresis in children.
Study Site	Endeavour College of Natural Health, Level 2/269 Wickham St, Fortitude Valley QLD 4006
HREC Approval Number	ETH17-1926
Principal Investigator	Dr Amie Steel
Chief Investigator	Dr Janet Schloss
Co-Investigator(s)	Ms Helen Heathwood

This is an invitation for the child in your care to participate in this clinical trial because it has been identified that they have issues with bed wetting. The research trial is testing a herbal treatment currently available for bed wetting, or a condition that is medically known as nocturnal enuresis. The treatment is called *Bedtime Buddy* and is a capsule that contains three herbs in a formulation of; Crataeva nurvala, Equisetum arvense, and Lindera Aggregata. This Participant Information Sheet will explains to you about the research project. It explains the treatments and procedures that are involved for the child as the participant and yourself as the carer of the child. Knowing what is involved will help you decide if you want the child to take part in the research.

Please read this information carefully and ask questions about anything that you don't understand or want clarification. Before deciding whether or not the child can take part, you might want to talk about it with a relative, friend or the child's local doctor.

Participation in this research is voluntary. If you do not wish the child to take part, they do not have to. The child will receive the best possible care whether or not they participate.

If you decide you want the child to take part in the research project, you will be asked to sign a consent form. By signing it you are telling us that you:

- Understand what you have read
- Consent to the child taking part in the research project
- Consent for the child to have the treatment that is described
- Consent to the use of the child's personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

What is the purpose of this research?

Bed wetting or the medical term 'nocturnal enuresis' is a form of night time urinary incontinence occurring in younger children. There are many factors that can contribute to this condition which can affect up to 20% of children over 5 years old. There are many different treatment strategies that you may have already tried with your children to address this issue. Complementary Alternative Medicine (CAM) treatments offer potential benefits but need to be tested under scientific conditions to determine if they work and are safe. It is well documented that children have improved self-esteem, self-concept and self-care if they are able to reduce or resolve bed wetting issues. This leads to improvements in social relationships with family and peers.

The main aim of the study is determine how effective a herbal capsule (listed by the Therapeutic Goods Admistration –TGA) is at reducing or stopping bed-wetting at night by children. The target population for this study will be children aged 6 to 14 years old both male and female. (ARTG Identifier: 290162)

The study also will measure; any day-time symptoms of urinary incontinence and also explore how bed-wetting may affect your child's psychosocial health. There are no single treatments effective at stopping bed-wetting completely. Traditional herbal medicines have been used in the past to treat children with bed-wetting issues with varied effects. Small trials have shown some promising outcomes and increased benefits with using herbal medicine to treat bed-wetting. Other treatments have shown improvement in reducing the number of wet nights but have been shown to relapse after stopping active treatment. Given that prescription pharmaceutical and herbal medicines are used cautiously in children and have potentially have undesired side effects. Controlled clinical trials are needed to explore CAM treatments such as herbal medicine for safety and effectiveness.

What is different with this trial is that it is specifically looking at potentially reducing the issue of relapsing symptoms so the child does not need to take the treatment long term. It also takes a holistic approach to how the issue is affecting the quality of life of the child, and if reducing bedwetting symptoms improves this health domain of their life.

What does participation in this research involve?

Once you have read this participant information sheet and have had the opportunity to discuss it with other people, the researcher will call you in several days to a week.They will check that you understand what the participation involves for your child and yourself.The researcher will then ask you a few screening questions to determine eligibility of the child, and if they are eligible to participate, a date will then be booked for the first (baseline) appointment.

Participation in this trial will require you and your child to visit the clinic at Endeavour College of Natural Health at 815/825 George St Haymarket NSW 2000for 3 appointments. The first visit is to enrol the child and complete a questionnaire and collect health data by the researcher.It will take approximately 60 minutes. At that time the child will have the weight and height measured and randomised to either the herbal capsule group or placebo capsule group. The dose of capsule will depend on the child's weight. A participant diary will be given to you and the child, as access to an electronic ediary via a link on a widget put on your Smart phone, or a paper diary to complete daily at home for duration of the trial. This records the episodes of urinary incontinence and daily fluid intake by the child.

The answers recorded in the diary will be used to measure; any abnormal symptoms experienced and the impact on the bedwetting.

The herbal capsule/s are taken once daily, every morning for a period of 8 weeks. At the second appointment at the college (Week 4), you will return the capsule bottle and any unused capsules together with the diary, and receive another 4 weeks supply. This appointment is approximately 30 minutes long. The final appointment occurs at Week 8 to complete the first part of the study. The herbal capsule bottle and remaining capsules will be returned and the parent, questionnaire completed again, and a feedback and evaluation form completed. There are several follow up phone calls during the time the capsules are taken, and after the capsules are completed (Week 8) to monitor any health changes to the child's condition.The timeline of visits and phone calls are as follows;

Baseline visit	• Parent & child
For three (3) days after commencing on the trial the RN will contact the parent via SMS or email daily	
Week 2 phone call	• Parent
Week 4 visit	• Parent & child
Week 6 phone call	• Parent
Week 8 visit	• Parent & child

Follow up phone calls for follow up at the 1st and 2nd month and final clinic visit at the 3rd month with both parent and child

The child will be participating in a randomised placebo-controlled research project. The reason for this is to determine if the product does work or not. To try to make sure the groups are the same, each participant is put into a group by chance (random). There is a 1 in 2 chance the child will receive the investigational product or the placebo. A placebo is a medication with no active ingredients or a procedure without any medical benefit. This is a blind study which means it will not be known which of the treatments the child is receiving.

Access to the Endeavour Sydney campus is most accessible by train or bus. There is a train and bus station across the road. To compensate for travel to the campus, each participant will be issued with fifty ($50) dollars equivalent in 2 vouchers that can be used universally at any retail outlet. They will be distributed to the parent as follows; Week 8 (at visit-$30) and Week 32 (posted - $20). They are to compensate you for your travel and commitment time in completing the diaries.

It is desirable that the child's local doctor be advised of your decision for the child to participate in this research project. If the child has a local doctor, we strongly recommend that you inform them of the child's participation in this research project.

What does the child have to do?

The child takes the capsule/s every morning with food. There are no lifestyle or dietary restrictions on the child and they are able to take their regular medication. There should be no impact on the child's lifestyle apart from the 3 clinic visits and taking the herbal capsule every morning.

What does the parent/carer have to do?

The child or parent will complete the diary daily, it includes a record fluid intake, episodes of night time incontinence and a record of taking the herbal capsule. There is a responsibility of the parent/guardian /participant to ensure the investigational product is taken regularly and in accordance with the instructions provided.

Other relevant information about the research project

This is the first clinical trial of this product in children. The same formula (called Urox) has been trialled in one study with 150 adults with urinary incontinence. The results showed significant improvements in participants' perceptions on the impact of urinary symptoms after 8-weeks of the treatment, compared to placebo. The results also showed a large effect on all urinary symptoms (day frequency, nocturia, urgency, stress incontinence and total incontinence) except day urgency incontinence.

Does the child have to take part in this research project?

Participation in any research project is voluntary. If you do not wish for the 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 the child from the project at any stage. Your decision that the child can or cannot take part or withdraw, will not affect their routine treatment, relationship with those treating them, or their relationship with the Endeavour college of Natural Health.

What are the alternatives to participation?

There are a variety of different treatments for bed-wetting available. Other options are available and you may have tried some of these in the past and include; prescribed medication, alarm therapy, bladder re-training, rewards for dry nights, hypnosis, acupuncture.

What are the possible benefits of taking part?

We cannot guarantee or promise that the child will receive any benefits from this research; however, possible benefits may include; reduced episodes of bed wetting and / or reduced episodes of day time incontinence, and improvements in social and psychological aspects of the child's life that are impacted upon by bed-wetting.

What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. The child may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If the child has any of these side effects, or you are worried about them, call the study researcher. There may be side effects that the researchers do not expect or do not know about. These symptoms will be recorded in the diary, however, if it is serious call the study researcher immediately about any new or unusual symptoms that the child experiences. Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, the study researcher may need to stop the child's treatment. The child's study researcher will discuss the best way of managing any side effects with you.

Safety data on the herbal capsule when taken in the adult trial (Urox) showed minimal adverse events. There are no documented interactions with any other medication. If there is a need for the participant to be treated medically for any side effects from taking the intervention, they can access the local doctor for a more comprehensive assessment. The Researcher can refer you if needed as well. Adverse Events reported from the clinical trial in adults with Urox (the same formulation as Bedtime Buddy) include:

- Episodes of diarrohea
- Urinary tract infection
- Flatulence

There is a potential that at the first visit to the clinic, the researcher may uncover a potential medical condition not previously identified by the parent or medical practitioner. The researcher is a registered nurse and is competent and skilled to assess the participant.

What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the study researcher will tell you about it and discuss with you whether you want the child to continue in the research project. If you decide that the child can continue in the research project, you will be asked to sign an updated consent form.Also, on receiving new information, the study researcher might consider it to be in the participant's best interests to withdraw them from the research project. If this happens, the researcher will explain the reasons and arrange for the participant's regular health care to continue by sending an updated letter to the child's local medical practitioner.

Can the child have other treatments during this research project?

Whilst the child is participating in this research project, they can take all of their regular medication or treatments. It is important to tell the researcher and the study staff about any treatments or medications the participant may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell the researcher about any changes to these during the child's participation in the research project.

What if I withdraw the child from this research project?

If you decide to withdraw the child from the project, please notify a member of the research team as soon as possible. This notice will allow the researchers to mention any symptoms related to stopping the capsules and to complete a Participant Withdrawal form, which will be posted or emailed to you. Please note that personal information collected before withdrawal will still be used for analysis but no further information will be collected.

Could this research project be stopped unexpectedly?

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

- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing
- Decisions made by the sponsor or by local regulatory/health authorities.

What happens when the research project ends?

The interventional treatment will be completed at 8 weeks. Part of this clinical trial is to determine if the study drug is able to prevent the symptoms of bed-wetting re-occurring as other treatment strategies have not been reliable in permanently stopping the freqeuency of bed-wetting. The whole trial is anticipated to take 12 months to complete. If you would like a copy of the summary of results when the trial is completed, a copy will be posted to the address you provided on enrolment into the study. The product is listed by the TGA and retail price is $32.95 for 30 capsules, which is 2-4 week supply depending on the weight of the child. It currently is available to purchase through some pharmacies. The company (Seipel Group) who manufacture the capsule will provide each participant with a 2-month supply of Bedtime Buddy at completion of the trial, and distributed at the final visit at the 3rd month follow up.

What will happen to information about the child?

By signing the consent form you consent to the researcher and relevant research staff collecting and using personal information about the child for the research project. Any information obtained in connection with this research project that can identify the child will remain confidential. The child's identity will be protected by the use of a Study number and participant code on all the documents. There will be a password-protected electronic file which contains both the child and parents' names, contact details for phone number and local medical officer. This will be kept on a password-protected computer in the researchers' locked office.The electronic and physical data will be stored for 15 years and then permanently deleted and destroyed.

The child's information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. It is anticipated that the results of this research project will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that the child cannot be identified, except with your permission. In accordance with relevant Australian and Queensland privacy and other relevant laws, you have the right to request access to the participant'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 the participant's information.

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.

Who has reviewed the research project?

This research project is being conducted by; Dr.Janet Schloss, PhD. It hassbeen funded through the University of Technology, Sydney and Endeavour College of Natural Health by both; an Innovations Connection Grant, awarded by the Dept of Industry, Innovation & Science (Federal Gov't) and Seipel Group Pty Ltd (ACN 152 681 028), PO Box 3449, Newmarket, 4051, Queensland, Australia. This research is being conducted by Endeavour College of Natural Health and sponsored in Australia by Seipel Group, PO Box 3449, Newmarket, 4051, Queensland, Australia

Declarations

The Sponsor (Seipel Group) will have no involvement at all with the trial design, clinical trial management and analysis of the trial results. Seipel Group is a commercial company who manufactures the herbal capsule and is partly funding the clinical trial with a commercial financial interest in the outcomes of the trial. Endeavour College of Natural Health is conducting the clinical trial completely independent of any relationship with Seipel Group and has no conflict of interest.

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 University of Technology, Sydney.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.

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 or if the participant has any medical problems which may be related to their involvement in the project (for example, any side effects), you can contact the Principal research investigator.The Principal investigator will then notify the Safety Committee and the approving HREC

Principal Researcher

Name	Dr Janet Schloss (PhD)
Position	Clinical Trials Coordinator
Telephone	+61 7 3253 9579 **(24 hours for adverse reactions – 0419 656108)**
Email	trials@endeavour.edu.au

If you have any questions about being a research participant in general;:

Clinical contact person

Name	Ms.Heather Heathwood
Position	Research Investigator / Research Assistant
Telephone	0466 941057
Email	trials@endeavour.edu.au

Any complaints about the way the research is being conducted; Complaints contact person for HREC

Name	University of Technology, Sydney- HREC,Racheal Laugery
Position	Ethics Secretariat
Telephone	02 95149772
Email	Racheal.Laugery@uts.edu.au

Local HREC Office contact

Name	Courtney Snow
Position	Research Ethics and Governance Adminstrator, Office of Research - Endeavour College of Natural Health
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