**Clinical Trial Protocol**

**Physiological, Psychological, Psychiatric, Surgical or Health Interventions**

**Evaluation of feasibility and effectiveness of the Mindgardens Functional Neurological Symptom Disorders (FND) Tic clinic.**

**Version 1.0, 7th July 2022**

**Professor Valsamma Eapen**

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# **General Information**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Protocol Title** | | | | | | | |
| Evaluation of feasibility and effectiveness of the Mindgardens Functional Neurological Symptom Disorders (FND) Tic program for children and adolescents. | | | | | | | |
| **Protocol identifying number** | HC220362 | | | | | | |
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| **Clinical Trial Sponsor** | | | | | | | |
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| **Human Research Ethics Committee** | | | | | | | |
| **Name** | | | UNSW HREC | | | | |
| **Status of ethical review** | | | **Approved**  **In progress**  **To be submitted** | | | | |
| **Trial Sites** | | | Site 1: Academic Unit of Child Psychiatry (AUCS), Psychiatry and Mental Health  School of Clinical Medicine, UNSW Medicine & Health  Level 3 AGSM, UNSW SYDNEY, NSW 2052 | | | | |
| **Funding for the Clinical Trial** | | | | | | | |
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| **Amount of Funding** | | | $100,000 | | | | |
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| **Insurance for Clinical Trial** | | | | | | | |
| **Insurer** | | | Newline Australia Insurance Pty Ltd – Via UNSW | | | | |
| **Type of Insurance** | | | Clinical Trial | | | | |
| **Confirmation of Insurance** | | | **Attached**  **In progress**  **To be submitted** | | | | |

# **Safety and Monitoring Contacts**

|  |  |
| --- | --- |
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| **Independent Safety Monitoring Board or Data Safety Monitoring Board Members** | |
| * List the members of the safety monitoring board. | |
| **Trial Management Group** | |
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# **Delegation of Clinical Trial Duties**

Responsibilities for the conduct and oversight for the trial are delegated to Professor Valsamma Eapen the Coordinating Principal Investigator. Trial related responsibilities will be delegated to the listed Principal Investigator(s) and any trial-related personnel. All trial-related duties delegated by the Coordinating Principal Investigator or Principal Investigator(s) and trial-related personnel must only be delegated to those that are qualified by experience and training. Delegated responsibilities will be retained in the [UNSW Clinical Trial Delegation Log](https://research.unsw.edu.au/document/Clinical%20Trial%20Delegations%20Log.docx). The UNSW Sponsor's Delegate is to be notified of the following:

* Protocol deviation reports are outlined in the UNSW Research Misconduct Procedure.
* Any serious breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Significant safety issues that are likely to (or have the potential to) affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Urgent safety measures implemented to remove or prevent a significant safety issue.
* Safety reports relating to the continuation, suspension, or discontinuation of the clinical trial for safety reasons.
* Non-compliance with the protocol, SOPs, GCP, and applicable regulatory requirement(s) significantly affects or can potentially affect human subject protection or reliability of trial results significantly.
* Participant complaints or concerns received concerning the conduct of the research.
* Significant modifications to the clinical trial are likely to affect a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Addition of participating trial sites, contractual arrangements at participating sites or modifications to legal agreements.
* The intention to conduct the trial in other countries.

# **Trial Objectives and Purpose**

The overall purpose of this study is to evaluate the effectiveness of an intervention program for children and adolescents with Tic Disorders.

Primary objectives

For children and adolescents attending the Mindgardens Functional Neurological Symptoms Disorders (FND) Tic program,

* To evaluate the effectiveness of an individualised, a brief cognitive behavioural intervention developed and delivered using standard clinical criteria for Tic Disorders for children and young people (12-18 years).
* To evaluate the effectiveness of a group intervention based on Comprehensive Behavioural Intervention for Tics (CBiT) for children and young people (8-12 years).

# **Background Information**

**Lay Project Summary**

To evaluate an individual intervention program for children and adolescents aged 12-18 years presenting with Tic Disorders and a group intervention program for children aged 8 to 12 years who present with Tic Disorders.

**Background**

Chronic Tic Disorders (CTD) and Tourette Syndrome (TS) are neuropsychiatric conditions characterised by the presence of motor and/or vocal tics for a minimum duration of 1 year [1-3]. Prevalence rates are around 3-5% for Chronic Tic Disorders and 1% for Tourette Syndrome [4, 5]. Around 90% of young people with CTD or TS present with a comorbid disorder, with ADHD and OCD being the most common comorbid conditions. Tic Disorders are a separate but related condition characterised by sudden and late-onset of tics, absence of a waxing and waning pattern, and often do not respond to pharmacological interventions[6, 7]. Previously considered a rare condition, there has been a rapid rise in functional Tic Disorder presentations since the COVID pandemic.

**Rationale**

There is a lack of coordinated service provision for children and adolescents in NSW and Australia with functional and Chronic Tic Disorders, hindering efforts to systematically collect clinical data that can be translated into gold-standard practice and shape service development. Clinical expertise in Tic Disorders, including Tic Disorders, remains limited to tertiary centres and primary and secondary care clinicians report feeling ill-equipped in caring for young patients [2]. Current service models cater poorly to young people with Tic Disorders (including Tourette Syndrome) where collaborative input in assessment and management planning is essential.

The proposed Mindgardens FND Tic program (for children and adolescents with Tic Disorders) is a tertiary assessment and intervention program for children and adolescents providing multi-disciplinary assessment and a brief intervention program for suitable patients. This program will see participants referred by their GP or specialist with a diagnosis of a Tic Disorder including functional Tic Disorder, Chronic Tic Disorder, or Tourette Syndrome. Two different streams will form part of this research study and are described below.

Such a program is not currently available in Australia in the public sector and is a significant gap in care provision for a group with high rates of physical and mental health (MH) morbidity, disability and healthcare utilisation[8].

**Significance, Innovation & Benefit**

Given the increasing morbidity rates among children and adolescents with a diagnosis of Tic Disorders and the potential perceived stigma and poor mental health literacy for accessing the healthcare system, children and adolescents attending this program will benefit from the specialised intervention leading to positive health outcomes. Additionally, this pilot work will also help inform health service practice, planning, and policy, and improve resource allocation and capacity building.

# .**Statement of Compliance**

The clinical trial will be conducted in compliance with the following guidelines and documentation:

* [ICH Guidelines for Good Clinical Practice (GCP)](https://www.tga.gov.au/publication/note-guidance-good-clinical-practice)
* [National Statement on Ethical Conduct in Human Research](https://nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) (National Statement)
* As approved by the Human Research Ethics Committee (HREC), the clinical trial protocol is responsible for monitoring the trial's conduct.
* The responsibilities set out by the UNSW Sponsors Delegate.

The onsite or remote monitoring standard operating procedures as put in place by the clinical trial sponsor.

# **Trial Design**

A randomised controlled trial (RCT) with children and adolescents 8-18 years with Tic disorder randomised to Stream one or Stream two of the study and their parents/caregivers of children aged 8-12 years.

A qualitative study that will involve group and individual sessions with children/adolescents and parents/caregivers was conducted as part of the RCT to develop practice and policy recommendations.

# **Sample Size**

The plan is to enrol 264 subjects to complete the trial. The nominated sample is based on n=1.962\*0.20\*(0.861)=264

0.052

There will be 88 subjects in each group.

# **Selection and Withdrawal of Subjects**

## **Inclusion Criteria**

Inclusion criteria for children and adolescents taking part in this study include:

1. Children and adolescents 8-18 years of age diagnosed with a Tic Disorder.

2. Referral from GP (a Mental Health Care Plan), Pediatrician, Psychiatrist or Neurologist

3. Tic Disorder as primary diagnosis/presenting problem

4. No further clinical investigations pending

5. Tics causing a significant impact on the functioning of a child or adolescent

6. Participants will be able to physically attend program sessions

7. Child and parent/carer consent to a referral to the program, assessment, and treatment

8. Commitment by referring specialist to stay involved in patient’s care after the study is

completed

Inclusion criteria for parents/caregivers taking part in this study include:

1. Parent/caregiver has a child or adolescent between the ages of 8-18 years of age diagnosed with a Tic Disorder.
2. The parent/caregiver receives a referral from GP (a Mental Health Care Plan), Paediatrician, Psychiatrist or Neurologist for their child to participate in the program
3. The parent/caregiver has a child with a Tic Disorder as a primary diagnosis/presenting problem
4. The parent/caregiver has a child that requires no further clinical investigations pending
5. The parent/caregiver has a child with a Tic diagnosis that causes a significant impact on the functioning of their child
6. The parent/caregiver has a child that will be able to physically attend program sessions
7. The parent/carer provides consent to a referral to the program, assessment, and treatment
8. The parent/caregiver receives commitment by their child’s referring specialist to stay involved in their child’s care after the study is completed

## **Exclusion Criteria**

Exclusion criteria for children/adolescents participants taking part in this study include:

1. Children and adolescents outside the age inclusion criteria as above

2. Significant cognitive impairment, learning or intellectual disability

3. Major mental illness leading to impairment in insight or judgment

4. Risk of harm to self or others as per consensus reached with the referrer

Exclusion criteria for parents/caregiver participants taking part in this study include:

1. The parent/caregiver has a child outside the age range for inclusion in the study as above
2. The parent/caregiver has a child with significant cognitive impairment, learning or intellectual disability
3. The parent/caregiver has a child with a major mental illness leading to impairment in insight or judgment
4. The parent/caregiver has a child which could cause be at risk of harm to self or others as per consensus reached with the referrer

## **Recruitment Strategy**

A referral pack, including an information sheet and referral form, will be distributed to medical specialists. The information letter will detail the minimum referral criteria for consideration in the study. The child’s local doctor (GP or specialist – paediatrician, neurologist) will complete the referral form and submit it to the FND Tic program for review.

Individuals referred will have an established diagnosis of a Tic Disorder made by the child’s local treating doctor (GP or specialist - paediatrician or neurologist). Patients and referrers will be informed that overall responsibility for ongoing management lies with the referring clinician. Referrals will be reviewed internally by the FND research study team at the weekly intake meeting for suitability against inclusion and exclusion criteria.

Following an initial assessment, clinical consensus will be sought for finalising treatment and management plans for each patient consistent with best practices in FND. This will include the determination of patients’ suitability to take part in a brief 10-week individual cognitive-behavioural intervention or group Comprehensive Behavioural Intervention for Tics (CBiT) on clinical grounds (motivation and aptitude, prior interventions completed, symptom profile) and not having any of the exclusion criteria. Suitable participants will be asked if they would be willing to complete the intervention should they wish to do so.

## **Screening**

Participants will be recruited based on the study’s inclusion criteria. Once a potential participant is determined to be eligible to participate by indicating their interest in participating in the study by contacting their child’s local doctor to have a referral sent to the study psychologist to indicate their interest. A member of the research team will undertake the consent process outlined below and will schedule/organise the data collection process by [e.g., arranging for the child and the parent/carer of the participant about when to come to the research site to participate in the FND Tic program].

## **Consent**

**Informed Consent Process**

Parents/carers of participants will be required to complete a consent form as part of entry onto the FND Tic program.

Online Surveys

The research team will engage with parents/carers of children and adolescents with a diagnosis of a Tic Disorder aged 8-18years to take part in online surveys.

Participants who complete the online surveys (parents/carers, children 12-18 years (children/adolescents 8-17 years will require the consent of the parent/carer) will provide “implied consent”. That is, by completing the online survey, these participants will be giving consent for their responses to the online survey to be used in the research. This will be explained in writing at the start of the survey; participants will also be assured at this point that participation is voluntary, and that data will be provided in an anonymous format.

Before participants (children/adolescents and parents/carers) complete the online surveys, they will be given a secure unique password-protected research study number by a member of the research study team. Access to online surveys will only require a unique identifying number for completion. No personal details will be required to be entered by the participant. We will link, via the de-identified unique number, to the patient’s details on the study’s Research Electronic Data Capture (REDCap) database. All information collected on participants for the research study will be treated confidentially. The researchers associated with this study will have access to data gathered from the data as part of the research study. REDCAP database will be used to house participant data.

The research team will engage with parents/carers of children with a diagnosis of a Tic Disorder to participate, on different occasions. It will be made clear to participants in our participant information sheets that they can stop participating in the study at any time if they experience discomfort or feelings of distress. The research team have extensive experience in engaging with children and young people. It will also be reiterated throughout the research study that participation is entirely voluntary, and participants will be advised that they have the autonomy to refuse participation in the study without consequences and that their future care provided will not be affected if they choose not to participate.

Reminders

In the absence of a response to the initial contact, reminder/follow-up contact with potential participants will be undertaken by sending reminder emails or letters on no more than two occasions and providing the parent/carer of consumers with a method of opting out of receiving further reminders.

## **Withdrawal of Consent or Participant**

Participants will be informed both verbally and in writing, the following consent into the study, that they will be freewithdrawawal from the study at any time and information regarding withdrawal from the study will be located at the end of the Participation Information Sheet. Participants will also be informed that non-identifiable online surveys completed before receiving an participant’s withdrawal form will be included in the research analysis. Participants who withdraw and are enrolled in the group sessions (children and adolescents aged 8-12 years) will have their data included in the research analysis, and the parent/caregivers will be advised verbally about withdrawal and their child’s information included in the research analysis before participating in this research activity.

However, participants involved in individual sessions may redact their transcripts following withdrawal from the study, however, their transcript will be held for five years but the data will not be included in the analysis. Subjects that withdraw from the study will not be replaced but will be included in the drop-out rate for the study. Subjects that withdraw from the study before the three month follow-up will not be contacted again.

# **Treatment** **of Subjects**

Please see below for details.

* 1. **Trial Intervention**

There will be two streams included in this research study.

Stream 1

The first stream will include children and adolescents aged between 12-18 years who have a diagnosis of a Tic Disorder (diagnosed by a GP or Specialists such as a Pediatrician, Psychiatrist or Neurologist).

Stream 2

The second stream will include children and adolescents aged between 8-12 years who have a diagnosis of a Tic Disorder (diagnosed by a GP, or Specialists such as a Pediatrician, Psychiatrist or Neurologist).

**Screening Process**

For children and adolescent participants to be allocated into a Stream (either Stream 1 or Stream 2), the following screening tools will be required for completion before the initial assessment. Responses to each measurement tool will be used to determine the allocation to each stream (Stream 1 versus Stream 2) that the child/adolescent will be allocated. The following screening table below (Table 1) highlights the required measurement tools to be completed for each of the following participants:

**Table 1: Screen assessment (Timepoint 1)**

|  |  |  |
| --- | --- | --- |
|  | **Screening activity before the initial assessment**  **(Timepoint 1)** | |
| **Name of Measurement** | **Child/Adolescent** | **Parent/Carer** |
| Yale Global Tic Severity Scale (YGTSS-Clinician) |  |  |
| Parent Tic Questionnaire (PTQ) |  |  |
| Beliefs about Tics Scale (BTS) |  |  |
| Child Behaviour Checklist (CBCL) |  |  |
| Revised Children’s Anxiety and Depression Scale (RCADS): Parent |  |  |
| Revised Children’s Anxiety and Depression Scale (RCADS): Child |  |  |
| Gilles de la Tourette Syndrome - Quality of Life Scale: Parent |  |  |
| Gilles de la Tourette Syndrome - Quality of Life Scale): Child |  |  |
| Multidimensional Assessment of Interoceptive Awareness: Youth (MAIA-Y) |  |  |

The research personnel responsible for administering or collecting data during the research will be the study clinical psychologist for this Project. She will be supported by the research assistant. Each intervention session for every patient will be delivered by the study clinical psychologist. If the study psychologist requires further clinical support, the Chief Investigatorator for the study will be available to provide clinical support, as the Chief Investigator and lead for this study.

Stream One

Table 2 below indicates activities associated with children and adolescents aged 12-18 years who have been diagnosed with a Tic Disorder and will consent to engage in the following research activities in conjunction with the individual psycho-cognitive behavioural intervention (CBiT) sessions.

**Table 2**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Activity** | **Research Activities to be completed** | | | | | **Follow-up** |  | |
|  | **Child/Adolescent** | **Parent/Carer** | **Clinician**  **(Study psychologist or PI for the study)** | **Initial Assessment**  **(Time point 2)** | **Post-Assessment**  **(Time point 3)** | **3**  **Months after baseline**  **(Time point 4)** | **Time taken to complete** | **Clinical data system** |
| Consent form |  |  |  |  |  |  |  | REDCap or paper medical record file |
| Individual Sessions (10 sessions over ten weeks)  Each session will take approximately 50 Minutes |  |  |  |  |  |  |  |  |
| Yale Global Tic Severity Scale |  |  |  |  |  |  | 25-30 minutes | REDCap  or paper medical record file |
| Parent Tic Questionnaire |  |  |  |  |  |  | 10 minutes | REDCap  or paper medical record file |
| Beliefs about Tics Scale (BTS) |  |  |  |  |  |  | 10 minutes | REDCap  or paper medical record file |
| Child Behaviour Checklist (CBCL) |  |  |  |  |  |  | 25-30 minutes | REDCap  or paper medical record file |
| Revised Children’s Anxiety and Depression Scale (RCADS): Parent |  |  |  |  |  |  | 10 minutes | REDCap  or paper medical record file |
| Revised Children’s Anxiety and Depression Scale (RCADS): Child |  |  |  |  |  |  | 10 minutes | REDCap  or paper medical record file |
| Multidimensional Assessment of Introceptive Awareness: Youth (MAIA-Y) |  |  |  |  |  |  | 10 minutes | REDCap  or paper medical record file |
| Clinical Global Impression Scale (CGI) |  |  |  |  |  |  | 5 minutes | REDCap  or paper medical record file |
| Tic Frequency Recording – Tic monitoring for parents |  |  |  |  |  |  | 10 minutes per day for one week | REDCap  or paper medical record file |
| Tic Motivation + Self Efficacy Questions (FND) |  |  |  |  |  |  | 5 minutes | REDCap  or paper medical record file |
| Parent Stress and Self-Efficacy Questions |  |  |  |  |  |  | 5 minutes | REDCap  or paper medical record file |
| The National Hospital Interview Schedule (NHIS) for the assessment of Tourette Syndrome (TS), Functional Tics and related behaviours |  |  |  |  |  |  |  | REDCap  or paper medical record file |

**Stream two**

Table 3 below indicates activities associated with children and adolescents aged 8-12 years who have been diagnosed with a Tic Disorder and will consent to engage in the following research activities.

**Table 3**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Activity** | **Research Activities to be completed** | | | | | | **Follow-up** |  | | |
|  | **Child/Adolescent** | **Parent/Carer** | **Clinician** | **Initial Assessment**  **(Time point 2)** | **Post-Assessment**  **(Time point 3)** | **3**  **Months after baseline**  **(Time point 4)** | | **Time taken to complete** | **Clinical data system** |
| Consent form |  |  |  |  |  |  | |  | REDCap or paper medical record file |
| Assessment session of 90 minutes  CBiT Group Sessions (10 sessions over ten weeks). Each group session will take approximately 90 minutes |  |  |  |  |  |  | |  |  |
| 4 x 90-minute parent group sessions run concurrently with the child group sessions (This would involve attending 4 sessions within the same time period as the child’s first group session) |  |  |  |  |  |  | |  |  |
| Yale Global Tic Severity Scale (YGTSS) |  |  |  |  |  |  | | 25-30 minutes | REDCap  or paper medical record file |
| Parent Tic Questionnaire (PTQ) |  |  |  |  |  |  | | 10 minutes | REDCap  or paper medical record file |
| Beliefs about Tics Scale (BTS) |  |  |  |  |  |  | | 10 minutes | REDCap  or paper medical record file |
| Child Behaviour Checklist (CBCL) |  |  |  |  |  |  | | 25-30 minutes | REDCap  or paper medical record file |
| Revised Children’s Anxiety and Depression Scale (RCADS): Parent |  |  |  |  |  |  | | 10 minutes | REDCap  or paper medical record file |
| Revised Children’s Anxiety and Depression Scale (RCADS): Child |  |  |  |  |  |  | | 10 minutes | REDCap  or paper medical record file |
| Clinical Global Impression Scale (CGI) |  |  |  |  |  |  | | 5 minutes | REDCap  or paper medical record file |
| Tic Frequency Recording – Tic monitoring for parents (Appendix K) |  |  |  |  |  |  | | 10 minutes per day for one week | REDCap  or paper medical record file |
| Tic Motivation + Self Efficacy Questions (FND) |  |  |  |  |  |  | | 5 minutes | REDCap  or paper medical record file |
| Parent Stress and Self-Efficacy Questions |  |  |  |  |  |  | | 5 minutes | REDCap  or paper medical record file |
| The National Hospital Interview Schedule (NHIS) for the assessment of Tourette Syndrome (TS), Functional Tics and related behaviours |  |  |  |  |  |  | |  | REDCap  or paper medical record file |

Different measurement tools will be offered at each of the four occasions to participants in both **Streams 1 and 2** as detailed in each of the tables above for children and adolescents as well as their parents/carers and the data will be routinely collected by the clinical team to track client outcomes and this data will be accessed in a de-identified form for evaluation.

Participants will be asked to complete the online surveys on different occasions. For adult participants, they will be invited to complete a set of questionnaires before the completion of the program (5 questionnaires will be completed) and on 2 occasions after their child completes the program (after their child’s first comprehensive assessment, at 3 months post-assessment) (a total of 15 questionnaires will be completed by the end of the study for this cohort). For children and adolescents aged 8-18 years, they will be invited to complete a set of questionnaires before the completion of the program (4 questionnaires will be completed) and 8 questionnaires on 3 occasions after the child/adolescent completes the program (after the child’s first comprehensive assessment, at 3 months post-assessment) (9 questionnaires will be completed).

Two reminders will be sent following initial contact, to complete the surveys before a participant will be considered lost to follow up. There will be a four-week period for a reminder from the initial contact and then a further four-week span from the second attempt to make contact. Each reminder will include instructions for participants to withdraw their consent to participate in future rounds of online surveys or from further contact.

**Measurement Tools**

**Yale Global Tic Severity Scale (YGTSS)** is used by the clinician and the parent/carer to provide an evaluation of the number, frequency, intensity, complexity, and interference of motor and phonic symptoms. The scale also gives an overall impairment rating.

**Clinical Global Impression Scale (CGI)**

The CGI is a measure of symptom severity and treatment response in consumers with mental health disorders. It is a brief 3-item observer-rated scale that can be used in clinical practice as well as in research to track symptom changes. The instrument can be used to provide clinical judgment-based assessment for determining the severity of symptoms and the treatment progress.

**Gilles de la Tourette Syndrome – Quality of Life Scale (GTS – QOL)** is a 28-item scale completed separately by the parent/carer and child about the child’s general quality of life about their Tics.

**Tic Self-Efficacy Scale** is afive-item scale completed by the child or adolescent which evaluates their control, frequency, and confidence of specific Tic Disorders.

**The revised Children's Anxiety and Depression Scale (RCADS-Parent**) is a 47-item scale that assesses the parent’s/carers understanding of their child’s symptoms around their anxiety and depression.

**Revised Children's Anxiety and Depression Scale (RCADS-Child)** is a 47-item self-reported questionnaire that assesses the child/adolescents’ understanding of their symptoms around anxiety and depression.

**Parent Tic Questionnaire** is a 14-item scale where the parent/carer reports the most common motor and vocal Tics experienced by their child over one week.

**Tic Monitoring Sheet for Parents** allows the parent/carer to monitor the number of times their child Tics in 10 minutes during the day over one week.

**Child Behaviour Checklist (CBCL)** is an 83-item scale completed by the parent/carer to detect the emotional and behavioural problems in their child.

**Beliefs about Tics Scale (BTS)** is a 20-item scale completed by the child or adolescent which assesses their beliefs associated with their tics.

**Multi-dimensional Assessment of Interoceptive Awareness - Youth (MAIA- Y)** is an 8-scale trait questionnaire with 32 items completed by children and adolescents toexplain what is going on in their bodies as they experience a Tic(s).

**Parent Stress and Self-Efficacy Questions** is a 3-item scale exploring how a parent/carer feels about their child’s tics.

**The National Hospital Interview Schedule (NHIS) for the assessment of Tourette Syndrome (TS), Functional Tics and related behaviours (NHIS) questionnaire** is completed by the clinician with the child/adolescent and assesses all different aspects of a child/adolescent’s tic.

# **Safety and Monitoring**

1. Assessment of Safety Event Report Forms

Safety reports will be assessed on the seriousness, causality, and expectedness of the event to the trial treatment(s), intervention(s), investigational medical product(s), investigational medical device(s). The following are known and expected adverse effects, harms, risks or discomforts associated with trial procedures, treatments or interventions.

1. Known Adverse Effects

We do not anticipate that participation in the study will have any negative impact on the physical or emotional wellbeing of the child/adolescent or parent/caregiver. However, occasionally a child may be momentarily distressed. In these cases, the parent/caregiver will be given a chance to settle their child, or to cease participation until they would like to resume.

1. Known Harms, Risks or Discomforts

Potential risk: There are no foreseeable risks to the participants associated with participation in this trial. There are no major risks to children/adolescents or parent/caregiver participants associated with participation in this trial. However, as children/adolescents or parents/caregivers participating in the RCT will complete measures about their/their child’s Tic condition, it is possible that answering these questions may cause distress to participants. Similarly, for the children/adolescents and parent/caregivers participating in group and individual sessions, answering questions and discussing their Tic/child’s Tic condition may cause participants to experience distress

Risk likelihood: Possible

Risk impact: Moderate

Risk mitigation strategy: To address the risk of potential distress to participants in the RCT, the following steps will be taken:

The chief investigator, will offer the family or adolescent the opportunity to speak with a psychologist who is not part of the study, and this will be organised by the Chief investigator for the study, and this will be at no cost to the family or participant participating in the study.

Contact details for a range of mental health support services and local services to support children/adolescents and parents/caregivers are provided to participants in the Participant Information Statement. These support services are independent of the research team and free of charge.

Participants are told in the Participant Information Statement (and at the time of each subsequent research activity) that they can stop participating at any time if they experience any feelings of distress.

Similarly, for the group or individual sessions, participants are told that they can stop participating at any time and contact details for a range of mental health support services and local services to support participants will be provided to them.

1. Adverse Events or Adverse Reactions

Adverse events (AE) are considered any untoward medical occurrence in a patient or clinical trial participant administered the intervention, which does not necessarily have a causal relationship with this treatment.

Adverse Reactions (AR) are considered untoward and unintended responses to the trial intervention related to any intervention procedures.

AEs and ARs are assessed using the safety monitoring flow chart. Those classified as "not serious" are assessed by the qualified physician/medical expert specified in section 2 of the protocol. The Qualified Physician cannot delegate this responsibility to other research personnel.

Adverse event reports must be reported to the Coordinating Principal Investigator as soon as the event occurs or within 48 hours of the adverse event ouccuring . All adverse event reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Serious Adverse Events

Serious Adverse Events(SAEs) that result in or lead to one or more of the following and the event is not related to the trial intervention:

* The death of a trial participant.
* A life-threatening illness or injury involving a trial participant.
* A participant's permanent impairment of body structure or body function.
* In-patient or prolonged hospitalisation (not for a pre-existing condition or an elective surgery) of a trial participant.
* Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or function of a trial participant.
* Fetal distress, fetal death or congenital abnormality or birth defect.

SAE reports are classified following the safety assessment flowchart and are assessed by Sponsors Independent Medical specified in section 2 of the protocol. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel. SAE reports are reported to the Coordinating Principal Investigator within immediately or within 48 hours of the event occurring at the clinical trial centre. SAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Serious Adverse Reactions

A Serious Adverse Reactions (SAR) is an SAE that is related to the trial intervention. SAR reports are classified following the safety assessment flowchart and are assessed by Sponsors Independent Medical specified in section 2 of the protocol. The sponsors independent medical expert must determine whether the SAR was expected or unexpected. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel.

#### **Expected Serious Adverse Reaction**

A serious adverse reaction by its nature, incidence, severity, or outcome is anticipated and identified in the current version of the intervention safety information are classified as a SAR report. SAR reports are reported to the Coordinating Principal Investigator within the timeframe that the serious event occurs. Serious Adverse Reaction reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

#### **Suspected Unexpected Serious Adverse Reaction (SUSAR)**

A serious adverse reaction by its nature, incidence, severity, or outcome is unanticipated and not identified in the interventions instructions for use or safety information are classified as a SUSAR.

Fatal or life-threatening Australian SUSAR reports are reported to the Coordinating Principal Investigator, the sponsor's delegate and the approving HREC within 7 calendar days after being made aware of the case follow up information reported within a further 8 calendar days.

All other Australian SUSAR reports are to be reported to the Coordinating Principal Investigator, the sponsor's delegate and the approving HREC within 15 calendar days after being made aware of the case follow up information reported within a further 8 calendar days. SUSAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Significant Safety Issue (SSI)

A safety issue that could adversely affect participants' safety or materially impact the trial's continued ethical acceptability or conduct. The Human Research Ethics Committee and Sponsor's Delegate must be notified of all significant safety issues within 15 calendar days of the sponsor instigating or being made aware of the issue**.** SSI reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

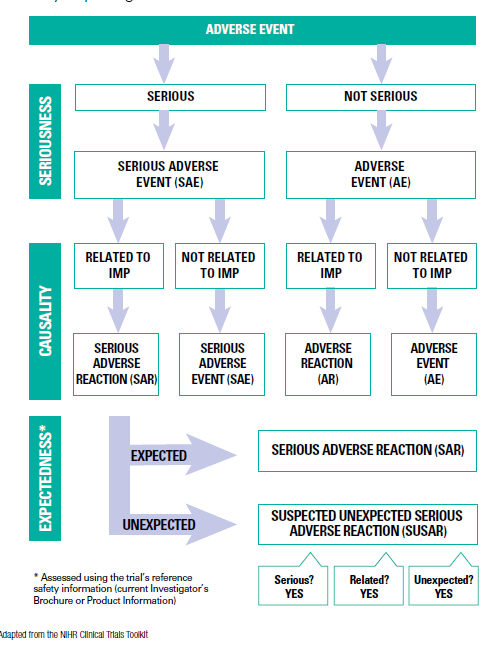
1. Urgent Safety Measure (USM)

A measure that is taken to eliminate an immediate hazard to a participant's health or safety. Significant safety issues where an urgent safety measure is required to be taken to eliminate an immediate hazard must be classified as a significant safety issue requiring an urgent safety measure. The Human Research Ethics Committee and the Sponsor's Delegate must be notified of any significant safety issues that meet the definition of an urgent safety measure should be notified within 72 hours. Examples include:

* a serious adverse event that could be associated with the trial procedures and that requires modification of the conduct of the trial
* a patient population hazard, such as lack of efficacy of an intervention used for the treatment of a life-threatening disease.

USM reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

1. Safety Assessment Flow Chart Investigational Medical Product Trials



1. Register of Clinical Trial Safety Monitoring Reports

A register of all event reports assessed and classified is to be retained by the Coordinating Principal Investigator and reported to the trial sponsor annually and the HREC if required.

1. Reporting of Clinical Trial Safety Monitoring Reports

Single case reports of Adverse Events Adverse Reactions, Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs), reports do not need to be reported to the UNSW Sponsor's Delegate or the HREC. All single case reports must be recorded in a safety monitoring register and are reported to the UNSW Sponsor's Delegate annually.

#### **Emerging Safety Issues**

The Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board is responsible for reviewing the safety information to identify any serious emerging safety concerns. If safety concerns are identified, this body will establish a plan to minimise the time participants may be placed at excess risk of harm. Before implementing the plan, the Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board must seek the advice of the human research ethics committee and sponsor's delegate.

#### **Annual assessment of safety**

The following information must be provided in a report to the sponsors delegate annually:

* Documented evidence that the Trial Management Group, Trial Safety Committee, or the Data Safety Monitoring Board (e.g. meeting minutes) confirmed that regular safety reviews occurred.
* Analysis of the trial intervention(s) and its implications for participants considering all available safety data and relevant clinical or non-clinical studies results.
* Any reports of emerging safety issues and a description of any measures taken or proposed to minimise risks.
* A copy of the safety monitoring register.

# **Non-compliance, Protocol Deviation and Serious Breaches of Good Clinical Practice**

## **Protocol Deviation**

A protocol deviation is defined as any breach, divergence or departure from the requirements of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that does not have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the research or clinical trial. Protocol deviations are events that do not occur persistently or systematically and do not potentially result in participant harms. Examples of protocol deviations include but are not limited to:

* Deviations because of participant adherence to the protocol, including rescheduled study visits, participants’ refusal to complete scheduled research activities or failure to complete self-report questionnaires required by the study protocol.
* Blood samples obtained or clinical trial testing occurring at times close to, but not precisely at the time points specified in the protocol.
* The completion of consent forms, safety monitoring reports, case report forms or data collection tools in a manner that is not consistent with the protocol instructions or failure to make reports within the required reporting timeframes.
* Administration of the clinical trial investigational medical product or device in a manner that is not consistent with the manufacturer's instructions for use.
* Use of an unapproved version of the participant information statement or recruitment of participants using unapproved recruitment procedures.
* Inclusion of a participant that does not meet the inclusion criteria.
* An urgent safety measure must be taken to eliminate an immediate hazard to a participant's health or safety.

## **Serious Breach of Good Clinical Practice**

A serious breach is defined as a breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial. Examples of serious breaches include but are not limited to:

* Persistent or systematic non-compliance with the instructions for completing consent forms, safety monitoring forms, case report forms or data collection tools that result in continued missed or incomplete data collection.
* Failure to record or report adverse events, serious adverse events, suspected unexpected serious adverse reactions, and significant safety issues where urgent safety measures were implemented.
* Failure to conduct clinical trial procedures following the clinical trial delegation log.
* Widespread and uncontrolled use of protocol waivers affecting eligibility criteria, which leads to harm to trial subjects.
* Failure to report investigational medical product or device defects to the clinical trial sponsor or any relevant regulatory body.
* Failure to conduct research following the issued approvals, permits or licences by required laws, regulations, disciplinary standards, and UNSW policies relating to the responsible or safe conduct of research.
* Concealing or facilitating breaches (or potential breaches) of the Research Code by others.
* Researching without the requisite approvals, permits or licences required by laws, regulations, disciplinary standards, and UNSW policies related to the responsible or safe conduct of research.
* Failure to conduct research as approved by an ethics review body where that conduct leads to (or has the potential to) result in participant harm.
* Researching without ethics approval as required by the National Statement on Ethical Conduct in Human Research where that conduct leads to (or has the potential to) result in participant harms.
* Any breaches as outlined in the UNSW Research Misconduct Procedure or the Australian Code for responsible conduct of research that leads to (or can potentially) result in participant harm.

## **Reporting Protocol Deviations**

* Protocol deviations occurring at a site must be documented in site files and reported by the principal site investigator to the Coordinating Principal Investigator.
* The Coordinating Principal Investigator must review the protocol deviation and the clinical trial protocol to establish the corrective actions and preventative steps to prevent the deviation from reoccurring.
* The protocol deviation and corrective action plan must be reported to the UNSW Sponsor's Delegate by the Coordinating Principal Investigator or Coordinating Research Team using the protocol deviation report form.

## **Reporting of a Serious Breach**

* The Principal Investigator must report a serious breach occurring at a participating site to the Coordinating Principal Investigator within a specified timeframe.
* The Coordinating Principal Investigator must review the serious breach, along with the clinical trial protocol, to develop a Corrective and Preventive Action (CAPA) that defines the steps to prevent the serious breach from reoccurring.
* The serious breach report and the CAPA must be provided to the approving HREC, and the UNSW sponsors delegate for review and approval.

## **Reporting of Serious Breaches by Third Parties**

* A Suspected Breach is a report judged by the reporter as a possible serious breach but has yet to be formally confirmed as a serious breach by the sponsor.
* A Suspected Breach form must be completed when a third party (e.g., individual/institution) wishes to report a suspected breach of Good Clinical Practice or the protocol and should be reported directly to the reviewing HREC without reporting through the sponsor.
* Recording of Protocol Deviation and Serious Breach Reports
* A register of protocol deviation and serious breach reports must be recorded. Written records and copies of documentation sent to the sponsor must be retained in the Investigator Site File.
* Copies of protocol deviation and serious breach reports must be recorded, written records and copies of documentation sent to the sponsor, referrals made to the HREC or establishing whether a breach of the Australian Code for Responsible conduct of research must be retained in the Master Site File.

# **Review of a Protocol Deviation and a Serious Breach**

* The UNSW Sponsor's Delegate will review reports to establish whether the event meets the definition of a protocol deviation or serious breach,  establish whether the proposed CAPA is appropriate and establish whether there is or will be ongoing impact reliability and robustness of the data generated.
* The UNSW Sponsor's Delegate will seek advice from the approving HREC on the corrective and preventive actions.
* Protocol deviation or serious breach reports where a UNSW researcher, staff or student is responsible for the protocol deviation or the serious breach will be reviewed as per the [UNSW Research Misconduct Procedure](https://www.gs.unsw.edu.au/policy/documents/researchmisconductproc.pdf) to establish a breach of the [UNSW Research Code of Conduct](https://www.gs.unsw.edu.au/policy/documents/researchcode.pdf) has occurred.
* Protocol deviation or serious breach reports where the UNSW Sponsor's Delegate determines that site personnel are responsible for a protocol deviation or the serious breach will be referred to their responsible institution for review under their Research Misconduct procedures to establish whether a breach of the [Australian Research Code for the Responsible Conduct of Research](https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018) has occurred.

# **Statistics**

We propose to evaluate the effectiveness of the Mindgardens Functional Neurological Symptom Disorders (FND) Tic program by examining the difference in the primary and the secondary outcomes before and after participants’ enrolment into the program (on entry into the Program versus post-assessment and 3 months after the initial assessment following the program) using appropriate statistical methods for different outcomes. We will use paired samples t-test to compare pre-versus post-intervention outcomes (e.g., Tic scores, quality of life scores) for each stream. Additionally, percent change at entry and completion of the program from baseline for efficacy variables will be analysed using analysis of covariance (ANCOVA) with respective baseline value as a covariate. Least-square means (LSM) and 95% confidence intervals will be evaluated from the ANCOVA. The data of percent changes will be assumed as normally distributed.

**Qualitative Study**

The transcriptions (redacted for any identifying information) will be coded using a thematic iterative analysis approach. NVivo Qualitative software will be used as a data analysis tool to code the themes that arise in the parent/caregiver focus groups and the professional/stakeholder focus groups. The Grounded Theory Method will guide the interpretation and thematic analyses of this data. Identified themes will be compiled into a coding frame and, as new themes emerge, they will be compared against the initial coding frame, and either added as new themes or used to expand and modify existing themes, until all data are accounted for. Data analysis will be undertaken using constant comparison methods and matrix displays will be used to explore similarities and differences across groups on key themes. Group and individual transcripts will be coded independently by two members of the research team to check the reliability of the coding frame. The data will be analysed using NVivo software for emerging themes on barriers and enablers, service uptake and satisfaction.

# **Data Ownership**

All research data collected during this trial is governed and handled following the Research Data Governance and Materials Handling [policy](https://www.gs.unsw.edu.au/policy/documents/researchdatagovernancepolicy.pdf). UNSW, rather than any individual or Organisational Unit, is the Custodian of data and materials and any information derived from the data. Original research data and primary materials generated in the research conducted at the University will be owned and retained by the University subject to any contractual, statutory, ethical, or funding body requirements.

# **Handling and Reporting Data**

Principal Investigators are responsible for maintaining adequate and accurate source documents and trial records that include all pertinent observations on each site's trial subjects. Source data must be attributable, legible, contemporaneous, original, accurate, and complete.

Trial subjects will be assigned a participant ID, and data will be reported using the electronic case report form. Data reported on the electronic case report form, derived from source documents, should be consistent with the source documents, or the discrepancies must be explained. Any change or correction to a [case report form] should be dated, initialled, and explained (if necessary) and should not obscure the original entry (i.e., an audit trail should be maintained); this applies to both written and electronic changes or corrections.

16.1 Direct Access to Source Data and Documents

Site principal investigator(s) and institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

**Randomised Controlled Trial**

The data will be held securely on a UNSW server that is password protected and only accessible to the Chief Investigators and research personnel. No external personnel will have access to the data. The majority of the data will be electronic, but there will be some paper files and data from these paper files will be entered into the study database, and paper files kept in locked filing cabinets in the Academic Unit of Child (AUCS), UNSW Medicine & Health.

For online surveys, the survey tool REDcap will be used to collect data, and the built-in audit trail will allow administrators to be able to determine all the activity and all the data viewed or modified by any given user. REDcap is a secure, encrypted online platform developed for the management of data projects. Only the research team listed in the application will have access to the REDcap account holding the data. Identifying information can be tagged as sensitive in REDcap and access further restrictions.

The electronic database for the RCT will be kept permanently and will not be deleted. It will be kept indefinitely in case it is of benefit for use in future research studies. The paper files will be kept for 25 years and will be deleted at the end of this time. The Dictaphone taped recording of the group and individual sessions will be deleted once all coding has been completed.

**Qualitative Study**

The audio recordings, with the use of a handheld Dictoaphoen, of the group and individual sessions will be deleted as soon as they have been transcribed. The redacted individual transcripts and electronic data will be kept for 5 years and will be deleted at the end of this time.

# **Monitoring Quality Control and Quality Assurance**

The Coordinating Principal Investigator and Principal Investigator(s) 'responsibility is to monitor the clinical trial. The Coordinating Principal Investigator and Principal Investigator(s) are responsible for undertaking or participating in site initiation or protocol-specific training before recruitment and data collection commences. A monitoring report demonstrating regular compliance monitoring with the clinical trial protocol, procedures, and HREC approval is provided to the UNSW Sponsor's Delegate annually.

Root, cause, and analysis reports are to be completed by the Coordinating Principal Investigator for reports of non-compliance and serious breaches. A corrective and preventative action plan must be developed and actioned for any reports of non-compliance and serious breaches.

# **Clinical Trial Research Agreement**

The Coordinating Principal investigators must ensure that agreements are executed at each of the following sites before site initiation, recruitment, and data collection commences.

# **Research Governance Site Authorisation**

Site authorisation is to be obtained, or if a research site is added, a site authorisation letter from the delegated authority of an institution responsible for any participating site is obtained. It is to be stored as a GCP essential document before participants are recruited at a participating site.

# **Good Clinical Practice Requirements**

It is recommended that the Coordinating and Principal Investigators ensure that all investigators and trial-related staff have current Good Clinical Practice Training. Once completed, the evidence of training confirmation is to be stored as a GCP essential document.

It is the responsibility of the Coordinating and Principal Investigators to familiarise themselves with the requirements of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)

# **Essential Documents for the Conduct of a Clinical Trial**

All essential documents referred to in section 8.2 of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)   are to be retained by all trial investigators.

# **Clinical Trial Delegation and Responsibilities Log**

| **Protocol / Study Number:** | HC220362 | **Sponsor Name:** | UNSW |
| --- | --- | --- | --- |
| **Principal Investigator Name:** | Professor Valsamma Eapen | **Site Number:** |  |
| **Site Name (if applicable)** | University of New South Wales | | |

**\*THIS FORM IS TO BE COMPLETED BY ALL PERSONNEL INVOLVED IN THE STUDY AFTER RECEIVING PROPER STUDY TRAINING AND BEFORE TAKING PART IN ANY STUDY ACTIVITIES**

**Principal Investigator (PI)**

By signing, I confirm/acknowledge that the tasks listed below will only be delegated to appropriately trained, skilled and qualified staff. I will remain responsible for the overall study conduct and reported data, ensuring study oversight. All associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations and have not performed any study tasks before appropriate delegation and completion of appropriate training. Mechanisms are in place to ensure that site staff receives the appropriate information and training throughout the study and that a 2-way communication channel exists between staff and self. Any changes in staff or delegation in staff will be recorded promptly.

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| **Name** | **Principal Investigator’s Signature** | **Initials** | **Start**  **(dd/mmm/yyyy)** | **End**  **(dd/mmm/yyyy)**  **(complete only if prior to end of study)** |
| Professor Valsamma Eapen |  | VE | 01/08/2022 | 31/12/2023 |
|  |  |  |  |  |

Site Staff

| **Name** | **Signature** | **Initials** | **Study Role** | **Key Study Task(s)**  **(choose from list below)** | **Start**  **(dd/mmm/yyyy)** | **End**  **(dd/mmm/yyyy) (complete only if prior to end of study)** | **PI Initials & Date**  **(dd/mmm/yyyy)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Dr Amanda Maxwell |  | AM | Study Psychologist | 1,2,3,4,6,7,8,15,18,19 | 01/08/2022 | 31/12/2023 | \_\_/\_\_\_/\_\_\_\_\_ |
| Dr Srilaxmi Balachandran |  | SB | Research Assistant | 2,15,18,19 | 01/08/2022 | 31/12/2023 | \_\_/\_\_\_/\_\_\_\_\_ |
| Professor Valsamma Eapen |  | VE | Chief INvestigator | 1,2,3,4,6,7,8,15,18 | 01/08/2022 | 31/12/2023 | \_\_/\_\_\_/\_\_\_\_\_ |
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| **Comments:** |
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| **Electronic Signature Declaration for Principal Investigator and Site Staff**   1. My electronic signature as it applies to entering electronic data or signing records in sponsor-owned or sponsor -outsourced computer systems is the legally binding equivalent of my handwritten signature. 2. I will not share password(s) assigned to me for this study with any other persons. |

|  |
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| **Principal Investigator's End of Study Declaration**  I hereby confirm that the above information is accurate and complete, and that I authorised the delegation of study-related tasks to each individual as listed above.  **Principal Investigator’s Signature:** **Date:** |

**Task Key:**

|  |  |
| --- | --- |
| 1. Obtain informed consent \* | 12. Sample collection |
| 2. Subject selection/recruitment\* | 13. Sample processing and/or shipment |
| 3. Confirm eligibility (review inclusion/exclusion criteria)\* | 14. Evaluate study-related test results \* |
| 4. Obtain medical history (source documents) | 15. Use IWRS/IVRS |
| 5. Perform physical exam\* | 16. Make entries/corrections on (e)CRFs |
| 6. Conduct study visit procedure as outlined in the protocol\* | 17. Sign- off (e)CRFs\* |
| 7. Make study-related medical decisions\* | 18. Maintain essential documents |
| 8. Assess AEs/SAEs\* | 19. Perform study-related assessments as per protocol \* |
| 9. Dispense study drug\* | 20. Complete company- specific log ( if applicable) |
| 10. Perform drug accountability | 21. Other (specify)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| 11. Study drug storage and temperature monitoring | 22. Other (specify) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

\*These tasks may only be performed by qualified individual as permitted by local law, medical or standard of care practices, or applicable required training as per job description or designation.

# **Safety Monitoring Register Template**

* [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx)
* [UNSW Adverse Event or Incident Event Case Report Form](https://research.unsw.edu.au/document/Adverse%20Event%20Incident%20Report%20Form%20September%202019%20.docx) Example.

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