Clinician Participant Information Sheet/Consent Form

Pharmacogenomics Study - *Adult providing own consent*

St Vincent's Hospital

Title	Towards Implementation of Pharmacogenomics-guided therapy in Patients with Mental Illness
Short Title	ENACT Stage 2 & 3
Protocol Number	2021/ETH00548
Project Sponsor	St Vincent's Hospital Sydney
Principal Investigator	*A/Prof Kathy Wu*
Associate Investigator(s)	*Dr Michael Millard, Prof Deborah Schofield, Dr Rupendra Shrestha, Dr Zhixin Liu, Dr Alison McLean*
Location	Departments of psychiatry at St Vincent's Public and Private Hospitals Sydney

Part 1 What does my participation involve?

1 Introduction

This is an invitation to take part in a pharmacogenomics research project. You are invited to take part because you are a psychiatrist who is currently involved in patient care for people with Major Depressive Disorder and/or Anxiety Disorder who are either inpatients or outpatients of St Vincent's Public Hospital and St Vincent's Private Hospital, or have patients external to these sites.

This Clinician Participant Information Sheet and Consent Form tells you about the research project. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Participation in this research is voluntary.

If you decide you want to take part in the research project, you will be asked to sign the consent form or provide verbal consent over the phone. By signing it you are telling us that you:
- Understand what you have read
- Consent to take part in the research project
- Consent to complete the clinician surveys and patient clinical data questionnaires
- Consent to arrange a buccal swab collection for your patient
- Consent to the use of your de-identified professional information as described.

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

2 What is pharmacogenetic research?

Genetic factors play an important role in how a person may respond to pharmacological medications. For example, genes may either reduce or enhance drug exposure and alter a person's response to drugs and their toxicity profile. Pharmacogenomics (PG) is the study of how genetic variants affect an individual's response to a drug.

Currently, researchers are studying genes to understand why people can have different responses to anti-depressive or anti-psychotic medications or why some medications do or do not provide active management of their symptoms of mental illness. Understanding a person's genes may provide an explanation for the individuals' response to medications. As each specific medication can be influenced by different genetic variants governing it's pharmacokinetic and/or pharmacodynamics responses, the results from multi-gene PG are weighted and combined to produce a composite predicted phenotype of response for each medication based on a patient's genotype.

PG-guided therapy has been shown to significantly enhance clinical outcomes in the field of mental health. PG-guided therapy aims to give the right drug at the right dosage to the right person at the right intervention time and potentially improve patient outcomes and provide cost savings in the mental health system.

3 What is the purpose of this research?

The ENACT trial is looking at how a simple genetic test (pharmacogenomics) through a buccal swab can help tailor antidepressant treatment to your patients.

The purpose of the research project is to investigate the feasibility of a patient-centred approach to mainstreaming PG-testing by non-genetics professionals in their clinical setting, using a model of care (MOC) that has been informed by the experience, attitudes and resource requirements of clinicians.

This study will look at the number of medication changes as a result of PG-guided care, as a primary objective. This is based on the rationale that PG will help you select the most suitable medication for your patient from the start to increase the chance of your recovery thus avoiding multiple medication trials and errors. Secondary objectives include response and remission rates at week 12 in patients taking psychotropic medications congruent with their pharmacogenomics profile versus incongruent medications; as well as the rate of medication adherence.

The study will also look at the cost effectiveness of the PG testing approach for selecting antidepressant therapy. A long-term goal of this project is to lobby for Medicare rebate status for pharmacogenomic testing to guide treatment(s) for major depressive disorder.

This research has been initiated by the study doctor, A/Prof Kathy Wu, Clinical Geneticist at St Vincent's Clinical Genomics, St Vincent's Hospital Sydney. This research has been funded by St Vincent's Health Australia Inclusive Health Program Grant. This research is a joint collaboration between the Departments of Clinical Genomics at St Vincent's Public Hospital and Psychiatry at St Vincent Private and Public Hospitals Sydney, University of NSW, as well as the Centre for Economic Impacts of Genomic Medicine at Macquarie University

4 What does participation in this research involve?

You have received this invitation because your patient has expressed interest in participating in this study as a patient participant, who has been determined to be eligible for the study by the Study Coordinator (SC). As part of the study participation, your patient is required to nominate their treating clinician (you) who will receive a copy of their pharmacogenomics report to guide the management of your patient.

If you agree to take part in this research project, as a clinician participant, your participation will include completing a Patient Clinical and Sociodemographic form (takes approx. 8-10 minutes) at baseline, a Clinician Participant Questionnaire (takes approx. 10-15 minutes). at Week 12 (Table 1). These questionnaires will be sent to you electronically by the study coordinator so you can complete them online.

You will need to collect one buccal (cheek) swab for pharmacogenomics testing from your patient either during your routine face-to-face clinic with your patient or a swab kit can be sent to their home for patient to self-collect a sample. If you are at SVH, you can contact the Clinical Genetics Advanced Trainee who can offer assistance with sample collection and if required, the study coordinator can arrange for a buccal swab kit to be sent to your patient's home (refer to the last page of the Clinician PIS for contact details). To protect your patient's privacy, the sample collected will be coded so no personal information is sent to the testing laboratory. The coded sample will be forwarded to the laboratory in the USA in a prepaid DHL Express package for PG-testing. The DNA sample will only be used for PG-testing and no other genetic testing will be carried out. The results from PG-testing generally takes around 5 – 7 days (from the sample being received in the laboratory in USA).

As per the model of care (MOC), the study coordinator will then arrange a multidisciplinary (MDT) telehealth clinic within one week of SVCG receiving the results (Figure 1). The MDT consists of geneticist/genetic counsellor, pharmacist/pharmacologist, you, and your patient. During the MDT clinic, guidance will be given by the SVCG team on how to interpret the PG report. As the treating psychiatrist, you will determine whether any changes to your patient's current medications are required based on the PG results, supported by the multi-disciplinary team and in discussion with your patient. The patient will receive their personalised PG result during the MDT telehealth appointment convened by St Vincent's Clinical Genomics (SVCG), St Vincent's Hospital, Sydney. A standard-of-care follow-up letter will be emailed to your patient and their primary physicians documenting the recommended medication changes (if any) based on the PG results.

We recommend that you advise your patient to inform their local doctor of their participation in this research project.

There are no costs associated with your participation, or your patient's participation, in this research project, nor will you/your patient be paid. The genetic test carried out as part of this research project will be provided to your patient free of charge.

Table 1: Study Schedule

Table 1	Stage 2							Stage 3
Visit Type	SCREENING	BASELINE	DAY 0	WEEK 2	WEEK 4	WEEK 8	WEEK 12	WEEK 24
Eligibility Assessment	✓							
Informed Consent	✓							
Clinical and Sociodemographic Data (**S2.1**)		✓						
PG Testing		✓						
PG result returned via MDT clinic			✓					
QIDS-SR16 (**S2.2.1**)		✓			✓	✓	✓	✓
DASS-21 (**S2.2.2**)		✓			✓	✓	✓	✓
AQoL-8D (**S2.2.3**)		✓			✓	✓	✓	✓
LCQ (**S2.2.4**)		✓					✓	✓
Work Productivity and Activity Impairment Questionnaire (**S2.2.5**)		✓					✓	✓
Three-Item Self-Rated Adherence Scale (**S2.2.6**)		✓		✓	✓	✓	✓	✓
ASEC (**S2.2.7**)		✓		✓	✓	✓	✓	✓
Medication Change Survey (**S2.3**)				✓	✓	✓	✓	
Psychiatrist Participant Questionnaire (**S2.4**)							✓	
MBS/PBS Claim Data								✓
GP Questionnaire (**S3.1**)								✓

Figure 1: Model of Care

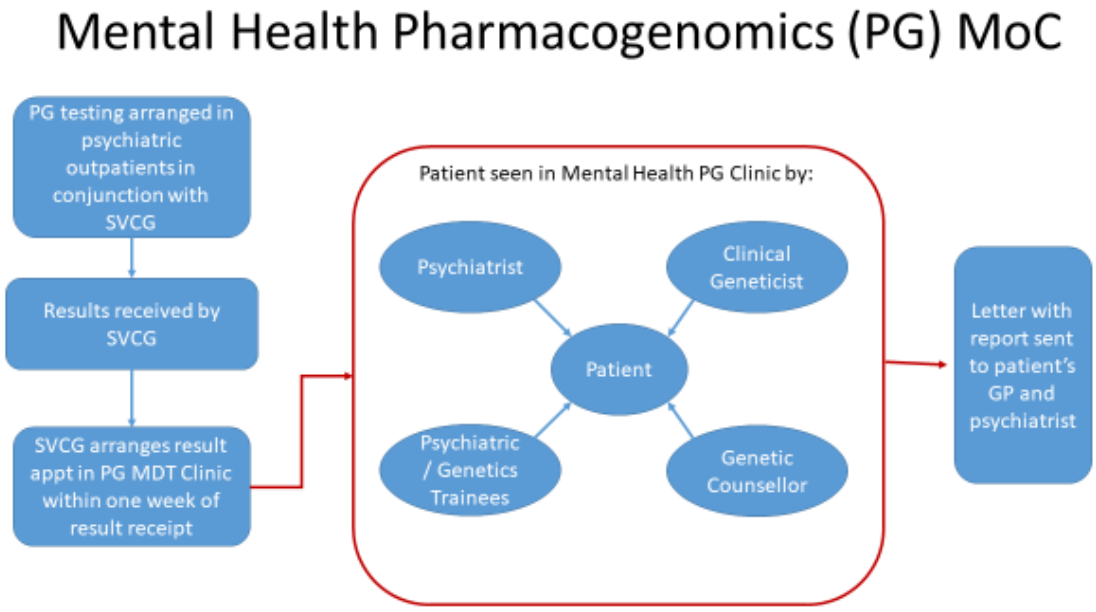
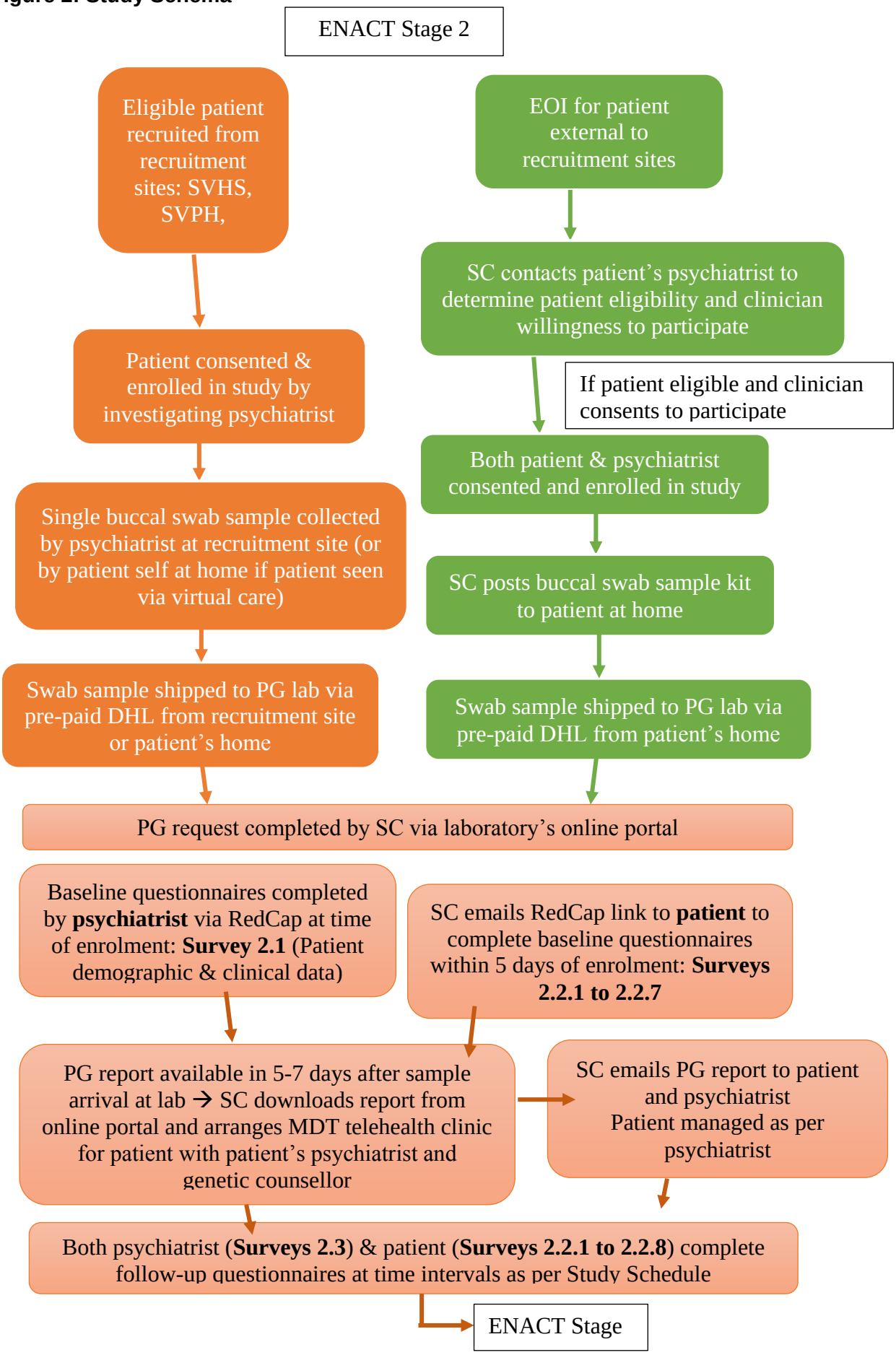
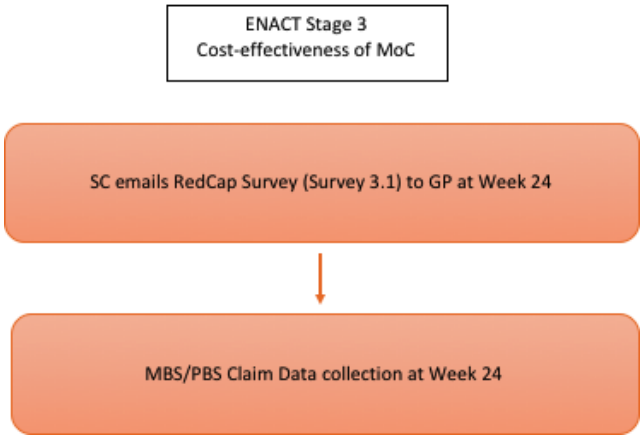


Figure 2: Study Schema





COVID VIRTUAL CARE CLINIC

Due to the global effect of COVID 19, you may be running your standard-of-care clinical visits virtually if agreed upon with your patient. You will still be able to enrol in this study as per below. If you wish to be involved and your patients wish to be involved verbal consent can be provided over the phone, and signed PISCF returned to the study coordinator electronically.

The buccal request form can be sent to your patient by the study coordinator so they are able to collect the standard of care buccal sample at home. The questionnaires will be emailed to you by the study coordinator.

5 What do I have to do?

There are no required changes to your routine clinical practice to take part in this study but you will be required to participate in an once-off MDT telehealth clinic with your patient, genetic doctor and genetic counsellor when your patient's PG report is available (Figure 1 and Figure 2)

If you have further questions about your patient's PG report during the study, the study doctor can be contacted for advice.

6 Other relevant information about the research project

This study aims to recruit 80 participants to undergo PG-testing and 10 – 20 psychiatrists from Departments of Psychiatry at St Vincent's Public and Private Hospitals Sydney: both inpatient wards and outpatient clinics, as well as external sites.

Patient and clinician participants will require access to a telephone and videoconferencing equipment (eg. Smartphone, tablet or laptop computer) to be able to take part in any of the study sessions that are not occurring face to face.

OneOme is a Clinical Laboratory Improvement Amendments (CLIA)-certified and College of American Pathologists (CAP) accredited PG laboratory based in Minneapolis, USA. CLIA/CAP accreditation represents the US equivalent of NATA/RCPA accreditation in Australia. The OneOme PG test includes 27 genes with high-level evidence of pharmacogenetic impact (PharmGKB and CPIC levels 1/A and 2/B), which cover over 200 medications, including approximately 24 anti-depressants, 3 anxiolytics, and 15 antipsychotics.

7 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to and if you decide to take part and later change your mind, you are free to withdraw from the project at any stage. In the case of your withdrawal from the project please contact the SC to discuss ongoing research involvement of your participating patient.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given or emailed a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your professional relationship with St Vincent Hospital or Clinical Genomics.

8 What are the possible benefits of taking part?

The possible benefits of taking part in this research may include a better response to antidepressant medication for your patient, where they experience less side effects and an improvement in their depressive symptoms. This research may also help to identify how we can pick the most appropriate antidepressant medication for people with moderate to severe depression in the future.

The data gathered from this research will provide valuable information that can be used to improve the treatment of Major Depressive Disorder and/or Anxiety Disorder, the access to PG-testing for psychiatrists and patients and improve patient's PG-testing experience.

9 What are the possible risks and disadvantages of taking part?

Genetic testing involves the study of genetic material (DNA) that is shared between blood relatives. The DNA sample will only be used for PG-testing and no other genetic testing will be carried out.

Genetic testing may raise important issues for your patient(s). A couple of potential issues to consider and be aware of are;

1. The PG-test result may give your patient uncertainties about current medications that have been prescribed. This uncertainty may also cause emotional stress.

2. The PG-result will be kept confidentially by the researchers and yourself as the treating psychiatrist. It is unlikely that statutory or contractual duties may require you as the psychiatrist and/or the researchers to disclose results of PG-tests to a third party (for example, insurance companies, employers, financial and educational institutions).

3. It is unlikely that PG results will impact your patient's ability to ascertain risk-based insurance*, as PG test does not predict disease risk.

*As of 1 July 2019, genetic testing will not impact on the ability of Australians taking up Life Insurance up to a certain limit, as part of the Financial Services Council's commitment to genetic inclusion. This Moratorium will be reviewed in 2023-24.

10 What will happen to your patient's test samples?

Your patient's buccal sample will only be used for the purpose of this research project. The DNA will be extracted from the buccal samples provided. The DNA sample will be used only for PG testing.

Your patient's de-*identifiable* DNA will be forwarded to an accredited clinical laboratory for PG-testing (OneOme Biotechnology Company in the USA). At the completion of testing, the DNA may be stored until the end of the project and will be destroyed in accordance to the local laboratory requirements. Privacy and confidentiality of stored samples will be maintained as per local laboratory regulation.

11 Will I be given the results of the research project?

It is anticipated that this project will be completed in 2024. If requested you will be provided with a summary of the research project.

12 Banking of Health Information

The information we collect from you and store in a secure electronic database for this research project is: your patient's clinical and sociodemographic information, including medication changes, as well as your experience using PG-testing as a treating psychiatrist.

We will not use any of this information for a different research project without the permission of a Human Research Ethics Committee. Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the research project may be presented in public talks or written articles but information will not be presented that identifies you or your patient.

Part 2 How is the research project being conducted?

13 What will happen to information about me?

By signing the consent form, you recognise that any information obtained in connection with your participation in this research project that can identify you will remain confidential.

Information about your participation in this research project will not be recorded in your employment records.

Your confidential record as a clinician participant will be kept in a secure electronic database housed at St Vincent's Clinical Genomics St Vincent's Hospital. Privacy will be ensured as per NSW Health regulations and the Human Genetics Society of Australasia (HGSA) guidelines. Your 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.

Your data will be stored in such a way that your identity could reasonably be ascertained. Only those persons authorised will have access to the information.

Any information collected and stored by the study coordinator relevant to this study during the research project may be reviewed for the purpose of verifying the procedures and the data. This review may be done by the ethics committee which approved this research project, regulatory authorities and authorised representatives of the Sponsor, Inclusive Health Program Grant, this organisation, St Vincent's Hospital, or as required by law. In these circumstances, the Sponsor will not collect (i.e. record) your personal information. By signing the consent form, you authorise release of, or access to, this confidential information as noted above.

In accordance with relevant Australian and/or NSW privacy and other relevant laws, you have the right to request access to your 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 information.

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 you cannot be identified, except with your expressed permission.

14 Who is organising and funding the research?

This research project is being conducted by A/Prof Kathy Wu, a Clinical Geneticist at St Vincent's Hospital Sydney. This research project is kindly funded by St Vincent's Health Australia Inclusive Health Program Grant.

15 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 St Vincent's Hospital 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.

16 Further information and who to contact

If you want any further information concerning this project or if you have any complaints, you can contact the principal study doctor below:

Name	A/Prof Kathy Wu
Position	Principal Investigator and Head of St Vincent's Clinical Genomics
Telephone	02-83824899
Email	kathy.wu@svha.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, please contact:

Name	Manager, St Vincent's Hospital Research Office
Telephone	02-83824960
Email	SVHS.Research@svha.org.au

To assist with obtaining your patients buccal swab during face to face clinical visit at St Vincent's Public and Private Hospitals only, please contact:

Name	Dr Alison McLean
Position	Co-Investigator and Clinical Genetics Advanced Trainee
Telephone	0414 707323
Email	alison.mclean@svha.org.au

To arrange for a buccal swab kit to be sent to your patients home, please contact:

Name	Ms Rosalind Moxham
Position	Clinical Genomics Study Coordinator
Telephone	8382 4898
Email	rosalind.moxham@svha.org.au

Consent Form

Title	Towards Implementation of Pharmacogenomics-guided therapy in Patients with Mental Illness
Short Title	ENACT Stage 2 & 3
Protocol Number	2021/ETH00548
Project Sponsor	St Vincent's Hospital Sydney
Principal Investigator	A/Prof Kathy Wu
Associate Investigator(s)	Dr Michael Millard, Prof Deborah Schofield, Dr Rupendra Shrestha, Dr Zhixin Liu, Dr Alison McLean
Location	Departments of psychiatry at St Vincent's Public and Private Hospitals Sydney

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my professional position or relationship with St Vincent's Hospital or Clinical Genomics.

I understand that I will be given a signed copy of this document to keep.

I understand that I can withdraw my consent to participate in this research project by completing a "Withdrawal of Consent" form.

Name of Participant (please print) _____

Signature _____ Date _____

Verbal consent provided YES / NO. Obtained by _____

Name of Witness* to Consent Process (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Coordinator/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Coordinator
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation

Title	Towards Implementation of Pharmacogenomics-guided therapy in Patients with Mental Illness
Short Title	ENACT Stage 2 & 3
Protocol Number	2021/ETH00548
Project Sponsor	St Vincent's Hospital Sydney
Principal Investigator	A/Prof Kathy Wu
Associate Investigator(s)	Dr Michael Millard, Prof Deborah Schofield, Dr Rupendra Shrestha, Dr Zhixin Liu, Dr Alison McLean
Location	Departments of Psychiatry at St Vincent's Public and Private Hospitals Sydney

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my professional position or relationship with St Vincent's Public or Private Hospitals Sydney.

Name of Participant (please print) _____

Signature _____ Date _____

Verbal withdrawal provided YES / NO

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Coordinator/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Coordinator/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, withdrawal from the research project.

Note: All parties signing the consent section must date their own signature