Government of South Australia | Health
Southern Adelaide Local Health Network

Participant Information and Consent Form

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Title	Transforming **C**ancer of **U**nknown **P**rimary with **I**ntelligent **D**iagnostics
Short Title	**CUPID study**
Protocol Number	2024 v2.1
Project Sponsor	Southern Adelaide Local Health Network Ltd (SALHN) Flinders Drive Bedford Park SA 5042
Principal Investigator	Professor Chris Karapetis
Site Principal Investigator	Professor Chris Karapetis
Location	Southern Adelaide Local Health Network

1. Introduction

Part 1: What does participation involve?

You are invited to take part in this research because you have been diagnosed with cancer, and the place in your body where the cancer started has not been identified by standard tests. This type of cancer is known as cancer of unknown primary (CUP).

We are doing this research to help find the best way to provide health care and improve outcomes for patients with CUP. The research project is trying to show whether new tests may help identify where the cancer started and identify features of the cancer that may play a role in how the cancer grows. We are studying whether we can identify genetic changes that may respond to anti-cancer medicines.

This Participant Information Sheet/Consent Form (PICF) tells you about the research project. It explains the research involved. 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. Before deciding whether to take part, you might want to talk about it with a relative, friend or local doctor.

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

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

- Understand what you have read.
- Consent to take part in the research project.
- Consent to the research that is described.
- Consent to the use of your personal information as described.

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

2. What is the purpose of this research?

The purpose of this research project is to determine the proportion of people with an initial diagnosis of CUP who then have a primary cancer site identified by further testing. This project also aims to examine the changes in the cancer that are found at the DNA level. This study will look at whether these molecular findings can help to determine where the cancer came from, and help to select a targeted therapy against the cancer.

Additionally, we will examine and care for you in line with the “Optimal Care Pathways” for people diagnosed with CUP. We will study whether following this guidance improves the accuracy of cancer diagnosis, reduces the number and type of diagnostic tests and health care visits, and improves patient health.

3. What does participation in this research involve?

If you agree to participate in this study, you will be asked to sign a consent form. We are seeking your approval to collect a sample of your tumour and a sample of your blood, and to share personally identifying and health information about you with the Australian Institute of Health and Welfare (AIHW) so that we can access de-identified information about your health and health service use. Access to your health records will be required to help us interpret the results; therefore, your participation will involve giving us permission to collect information about your cancer diagnosis and use of health services. This research will be monitored by Flinders Medical Centre Medical Oncology Department Clinical Trials unit.

Cancer cells have changes in their DNA (the "instruction book" for the cells in your body) that cause uncontrolled growth. When you were diagnosed with cancer, you had a piece of tissue removed from your tumour(s) (called a “biopsy”) to confirm what type of cancer it is. Testing on the tumour (somatic molecular profiling) may help identify where your cancer started.

Furthermore, the test may identify genetic changes in your cancer that may respond to anti-cancer medicines. Your doctor may then tailor your treatment accordingly. Treatment in this research project will be determined and given by your treating doctors. The trial does **NOT** provide treatment.

4. 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. If you decide that you can take part and later change your mind, you are free to withdraw from the project at any stage.

If you decide that you take part in this research project, you will be given this Participant Information Sheet and Consent Form to sign and you will be given a copy to keep.

Your decision whether you can or cannot take part or take part and then withdraw, will not affect your routine treatment, your relationship with those treating you, or your relationship with your treating doctors.

5. What are the alternatives to participation?

You do not have to take part in this research project to receive treatment. Other options are available, these include:

- Receive standard treatment for your CUP with your treating team without being in this study.
- Join a different research project.
- Receive no treatment.
- Receive comfort care (also called "palliative care").

Your treating doctor will discuss these options with you before you decide whether to take part in this research project.

6. **What are the possible benefits of taking part?**

Your health may or may not improve in this research project, but the information obtained from the study may help us to better understand the care patients receive when diagnosed with CUP, and results may help us to develop new tests that we can use to determine where the cancer started. These tests may also help us to select better treatments.

7. What are the possible risks and disadvantages of taking part?

7.1 Finding a suitable therapy which may not be accessible on the Pharmaceutical Benefits Scheme (PBS).

Your tumour tissue and blood samples will be tested through a laboratory. The findings from these tests will be discussed at a multidisciplinary meeting of medical professionals (Molecular Tumour Board). Your doctor will then be notified of the outcome from the Molecular Tumour Board. This information may be used by your doctor, with the advice of the Molecular Tumour Board, to assign the most appropriate therapy. However, this study does NOT provide your treatment/therapy. There is a chance that the tests may identify a suitable treatment for you, but you may not be able to access that treatment due to constraints from the PBS.

7.2 Possible risks associated with loss of privacy.

Although your genetic information will not contain any personal identifying information, through responsible data sharing it could be used to identify you and your blood relatives. Because some genetic differences can help to predict future health problems experienced by you or your blood relatives, this information might be of interest to healthcare providers, some insurance companies, and others.

It is possible that your genetic information would cause you or your family distress, such as by revealing that you or a blood relative has elevated genetic susceptibility to a certain disease.

Your privacy is very important, and Flinders Medical Centre uses many safeguards to protect your privacy. However, there is no guarantee that your identity will never become known, but we will be constantly vigilant.

8. What will happen to my test samples?

Blood and tumour tissue samples will be collected to determine the genomic profile of your cancer.

With additional approval by Southern Adelaide Clinical Human Research Ethics Committee, tumour tissue samples collected at screening may be used for future research related to CUP, for the evaluation of experimental drugs in disease therapy, and/or the development of diagnostic tests or tools that help with detecting or understanding of CUP. Your clinical data may also be used as part of such research, but none of the data ever presented or published will identify you.

If you decide not to take part in this study, or withdraw consent, your tissue sample will still be used for research. Your samples can be destroyed if you specifically ask for them to be destroyed.

All samples will be stored indefinitely but your samples can be destroyed upon your request or the request of a legally responsible family member.

9. **Can I withdraw from this research project?**

If you decide to withdraw from this research project, please notify a member of the research team before withdrawal. If you do withdraw consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with the law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want the results that have been collected already to be included in the research, you must notify the study doctor or relevant research staff.

10. What happens when the research project ends?

Participants will continue with their regular follow-up arrangements with their treating doctor after the project ends. When the research project is completed, participants may be provided with a summary of the results by their treating medical oncologist.

Part 2: How is the research project being conducted?

11. What will happen to my information?

- The data we will collect and store at Flinders Medical Centre will include your name, address, and date of birth. We will store this identifying information separately from your health information.
- At the time of sampling, we will assign you a unique number and attach this number, not your name, to your tumour tissue and blood samples, and health and health service information.
- The data will be kept in the Medical Oncology Research Unit and in a protected area where only research staff have physical access.
- Study electronic records will be stored on secure Flinders Medical Centre servers accessible only by approved research staff upon completion of two-factor authentication.
- The data and specimens that do not contain any identifying information will be shared with other investigators and treating clinicians involved in the study beyond Flinders Medical Centre.
- The data will be securely archived at Flinders Medical Centre for 15 years and then permanently deleted. By signing the consent form, you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. 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 health information will be obtained from your medical records held at this and other health services, for the purpose of this research. By signing the consent form you agree to the research team accessing your health records if they are relevant to this research.
- Your identifying health information will be shared with the Australian Institute of Health and Welfare (AIHW) for linkage with Australian and State and Territory government health records. We will then access information about your health and use of other health services using a secure remote access platform managed by a government agency (the Australian Bureau of Statistics). The information we access for this part of the research will not include any personally identifying information about you. At the completion of the study, this data will be securely archived for 7 years and then permanently deleted.
- It is possible the genetic profiling results might include information that could be useful for your family to predict future diseases, and this can be disclosed to them with your approval.
- It is anticipated that the results of this research will be published and/or presented in a variety of forums. You will not be identified in any of these publications or presentations.

- In accordance with relevant Australian and/or South Australian privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team member named at the end of this document if you would like to access your information.
- Any information obtained for the purpose of this research that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law. No personally identifying information will be shared other than for the purpose of data linkage.

12. Who is organising and funding the research?

This research project is being coordinated by the Medical Oncology Unit at Flinders Medical Centre.

The Medical Research Future Fund has provided a grant for the CUPID clinical trial to be conducted.

13. Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called the Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Southern Adelaide Clinical HREC and the South Australian Department for Health and Wellbeing HREC.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007; updated 2023). This statement has been developed to protect the interests of people who agree to participate in human research studies.

14. 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 you have any medical problems which may be related to involvement in the project, you can contact the CUPID study coordinator below:

Site Contacts:

Contacts:	**Telephone number:**	**Email address:**
Coordinators: CUPID study coordinator	(08) 8204 4835	Health.Cupid@sa.gov.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person:

Name	Manager, Research Governance and Ethics
Position	Director, Office for Research
Telephone number	(08) 8204 6453
Email address	Health.SALHNOfficeforResearch@sa.gov.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, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details:

Reviewing HREC name	Southern Adelaide Clinical HREC
Telephone number	(08) 8204 6453
Email address	Health.SALHNOfficeforResearch@sa.gov.au

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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 take part in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.
- I will be told the results by a doctor or a genetic counsellor, unless I decide that I do not wish to receive the results. Appropriate follow up care and counselling will be arranged, as necessary
- My genetic test results may have implications for the health/genetic risks of my family members.
- My genetic test results may affect my ability to obtain some types of insurance.
- My genetic test results can be used to inform the counselling and genetic testing of family members, though my identity will not be revealed to them.
- In the event of my death, I consent to share my results with: _____
- I understand that the samples, genetic data, and health information collected for the study may be stored in one or more national or international databases and will only be stored in a manner that will not identify me.
- I consent to the publication of my test results and medical information in scientific and medical articles that result from the research, on the understanding that my identity will remain confidential.
- I consent to the sharing of my data and sample(s) for use in ethically approved future research outside this study.
- I understand that I will be given a signed copy of this document to keep.
- I give permission for any previously collected tissue, blood samples to be used and shared with other investigators of the study beyond Flinders Medical Centre.
- I give permission for my doctors, other health professionals and hospitals or laboratories outside this hospital to share information with Flinders Medical Centre and the named investigators, concerning my condition, treatment, and use of health services for the purposes of this project. I understand that such information will remain confidential.

- I give permission for my personal and health information to be shared with the Australian Institute of Health and Welfare (AIHW) for the purpose of data linkage.
- I understand the researchers will access and analyse my health information without access to my name and other identifying information.
- I consent to have another biopsy if needed for analysis.
- I consent to have blood samples for research purposes.
- I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

• This specific research project	☐Yes ☐No
• Other research that is closely related to this research project	☐Yes ☐No
• Any future research	☐Yes ☐No

Name of Participant (please print)_____

Signature _____ Date _____

Under certain circumstances (see Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 at 4.8.9*) a witness* to informed consent is required.*

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witnesses 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 Doctor/Senior Researcher†

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

Name of Study Doctor/Senior Researcher† _____

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.

Participant Withdrawal Form

Title	Transforming **C**ancer of **U**nknown **P**rimary with **I**ntelligent **D**iagnostics
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Declaration by Participant

I wish to withdraw from taking part in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me, or my relationship with Flinders Medical Centre.

- My data may be used for the project, but I do not wish to participate any further in the CUPID study ☐Yes ☐No
- I agree for my tissue samples to be used for the research project ☐Yes ☐No
- I wish for all my data to be withdrawn from the study and my biological samples to be destroyed ☐Yes ☐No
- I withdraw my consent for the use of my tissue and blood samples in other research that is closely related to this project and any future research.

☐Yes ☐No

Name of Participant (please print)_____

Signature _____ Date _____

Under certain circumstances (see Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 at 4.8.9*) a witness* to informed consent is required.*

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witnesses 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.

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 Doctor/Senior Researcher†

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

Name of Study Doctor/Senior Researcher† _____

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.