Flinders University of South Australia and All India Institute of Medical Sciences (AIIMS)-Bhubaneswar.

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Bhubaneswar, India

Title	What is the effect of a dietary resistant starch intervention on the colonic luminal environment and HIV-related immunity and is a feeding trial feasible in HIV-positive adults in India?
Short Title	Resistant starch in HIV-positive adults in India.
Project Sponsor	Flinders University
Coordinating Principal Investigator/ Principal Investigator	Professor Paul Ward-Chief Investigator Assistant Professor Balamurugan Ramadass-Principal Investigator-India (PI-India) Ms Elissa Mortimer-Study Coordinator and Principal Investigator.
Associate Investigator(s)	Professor Geraint Rogers Professor Graeme Young Professor BS Ramakrishna
Location-where recruitment will occur -	Bhubaneswar, India

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. The research project is testing a treatment for symptoms of the gut which may be useful for people living with HIV. A food additive made from the maize plant called High Amylose Maize Starch or 'HAMS,' will be added to the normal diet because it is high in a nutrient called 'resistant starch.' This study is being done in India because in countries where the water and sewerage system is not that good, people who live there come into contact every day with bacteria that can lead to repeated infections of the gut. Research has shown that resistant starch can be of benefit when this happens. This Participant Information Sheet/Consent Form (PICF) tells you about the research project. It explains the tests and treatments 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 or not to take part, you might want to talk about it with a relative, friend or your local doctor.

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

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 have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this PICF to keep.

2 What is the purpose of this research?

Aim (1) To see what happens when HAMS is added to the diet by measuring changes in:

a. your stool;
b. your blood;
c. symptoms in your gut.

Aim (2) To explore the things that might make a study with HAMS easy or difficult for participants.

Significance: HIV disease and Anti-Retroviral Therapy (ART) for HIV can both cause gut problems in the stomach and intestines. New ways of managing these problems will be helpful to make patients feel better and help them to stay on their ART. This will decrease the chance of HIV infection being passed on to other people.

Dietary starch comes from plants like cereals and potatoes and provides a source of energy for the body. It is an important part of the human diet. Instead of being digested in the stomach and small intestine, resistant starch reaches the large intestine and is used by the bacteria that live there in a process called fermentation. This is thought to be good for the body. So far, studies with resistant starch have happened with children and adults in countries including India, Australia, England and the United States of America. Some studies have tested resistant starch mixed with other special food ingredients in HIV-positive participants but no studies have tested what happens when resistant starch by itself is added to the diet in HIV-positive people.

Resistant starch is considered very safe for consumption by humans and is found in the normal diet in foods like potatoes and bananas. Resistant starch as an ingredient has been used by bakers for many years because it makes bakery foods crusty. One example of resistant starch is HAMS which will be used in this study. HAMS has been given GRAS status (Generally Recognized As Safe) by the United States

of America Food and Drug Administration. This means it is allowed to be added to foods being eaten by humans. It is of natural origin from maize plants which have not been genetically modified.

The results of this study will be used by the study coordinator, Ms Elissa Mortimer, to obtain a Doctorate of Public Health degree. Ms Mortimer developed the idea for this study which is funded by Flinders University of South Australia with All India Institute of Medical Sciences (AIIMS) Bhubaneswar as the research partner.

3 What does participation in this research involve?

You will be participating in a 'double cross-over' dietary study. In a double cross-over study, different groups each have different treatments in turn separated by a period of normal diet. Following this, the whole process is then repeated. The treatments in this study are two different types of starch: HAMS and cornstarch. You will be asked to eat foods which have HAMS or cornstarch added to them. Cornstarch is digested by your body in the stomach and small intestines in the usual way that food is digested. Instead of being digested in the stomach and small intestine, HAMS reaches the large intestine where it is used as a food by bacteria that normally live there. These bacteria can do beneficial things in the human body which is why we are interested in studying the effect of HAMS on them. HAMS and cornstarch do not change the taste of food so you may not notice any difference compared to normal food.

The order in which participants consume the two starches will be chosen by chance (random). This is to try to make sure the groups are the same. There will be a break between the HAMS and cornstarch foods so that your body adjusts back to normal before you start the other starch. You will not know if you are consuming resistant starch or cornstarch. This research project has been designed in this way to make sure that participants give the most accurate responses to the questionnaires and that the researchers interpret the results in a fair way.

Initial steps

The research staff will explain the study to you using this PICF document. If you decide to participate, the research staff will ask you to sign the consent form. They will then ask you some questions in the screening step. If you meet the below and exclusion criteria, you will be able to participate in the study:

Inclusion criteria

1. HIV-positive adults aged 18 years or over on ART
2. CD4+ T cell count more than 200 cells/mm3
3. No antibiotics within last 6 weeks

Exclusion criteria

1. Other gut problems such as Crohn's Disease or Ulcerative Colitis.
2. Current participation in other research studies
3. Pregnant or breastfeeding.

This is a study with two parts: the first is the dietary part, the second is the interview or focus group part where the research team will ask participants the things that make this study easy or difficult. These two parts of the study will happen at the same time, during the 16 weeks that participants will be involved in the study.

Participants will be asked to give a stool and blood sample at day 0 and to complete a questionnaire about any gut symptoms so the researchers can see how these measurements change once the starches are added to the normal diet. Participants will be randomly put into one of two groups. The first group will eat HAMS added to their usual diet for 2 weeks then only their usual diet for 2 weeks then cornstarch added to their diet for the final 2 weeks. The second group will do this in the reverse order by eating the

cornstarch for 2 weeks then the normal diet for 2 weeks then the HAMS for 2 weeks. Following this, the whole process is then repeated. This is shown in the below Figure 1.

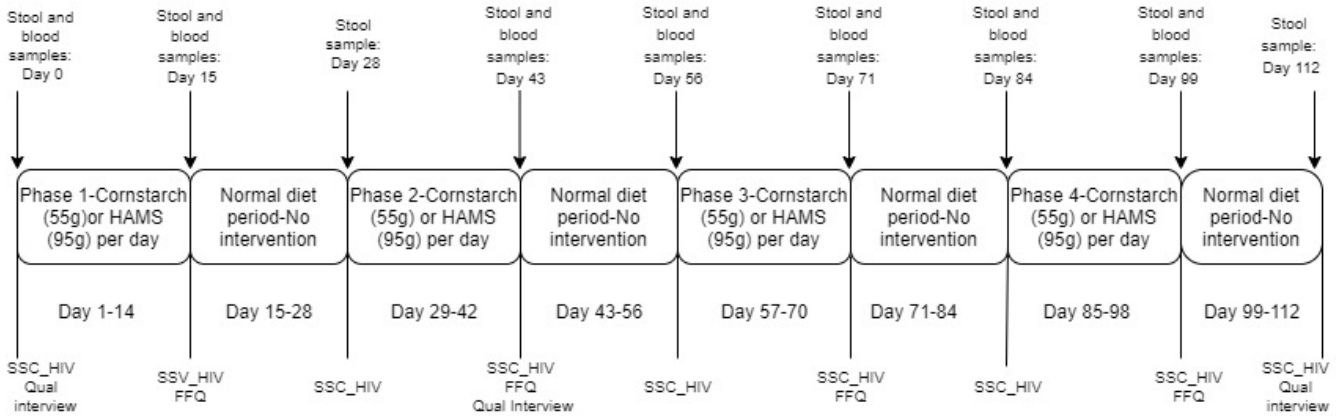

Figure 1: Study timing.

Participants will be provided daily with the study food containing HAMS or cornstarch. HAMS and cornstarch are a similar texture to wheat flour and do not have a strong taste. The study coordinator will test different study foods with a small group of 5 study staff first to work out which one tastes best and can be eaten for the study period.

Participants will be asked to provide stool and blood samples on the days shown in Figure 1. The research team will teach participants how to collect the stool samples and will then collect these samples from participants. Samples will then be frozen and transported to the laboratory for storage. The blood samples will be taken by a health worker employed by the ART clinic. Samples will be transported by the research team to the laboratory in vials labelled with the participant identifier code rather than their name.

There are no additional costs associated with participating in this research project, nor will you be paid. All of the study food and the cost of stool and blood tests required as part of the research project will be provided to you free of charge. The usual way you access drugs for your HIV such as ART will not be affected.

You may be reimbursed for any reasonable travel costs associated with the research study.

4 What do I have to do?

- You will be asked to eat the whole serve of the study food. The study food will be roti with HAMS or cornstarch added with the other ingredients. The total amount of time during which you will consume study foods is 8 weeks in total. The total amount of time you will participate in the study is 16 weeks. The details are provided in Figure 1.
- In total, 9 stool samples and 7 blood samples will be collected over the total 16 weeks.
- On collection days you will also be asked to complete the questionnaire which will ask about any side effects you may be experiencing. This will take 5-10 minutes to complete. Study staff can help you.
- On three days (days 15, 43 and 99), you will also be asked to complete a brief questionnaire about what you have been eating and drinking recently. This should take 10-15 minutes to complete. Study staff can help you.
- You will also be asked to participate in three interviews for the qualitative part of the study. You can choose if you prefer to have an interview by yourself or join 5 other participants for a focus group discussion. Both of these will be with a research staff member plus interpreter. The three interviews/focus groups will be held on:

- Day 0 immediately before phase 1 begins;
- Day 43; and
- Day 112.

The interviews and focus groups will be recorded (audio only) so that the discussion can be written down afterwards. The only people who will access these audio recordings are the interpreter and two members of the research team. The recordings will be kept in a locked filing cabinet when not in use.

After the interviews and focus groups are completed, participants will be invited to check the summary report written by the research team. The reports will be written in a way that keeps the identity of participants anonymous.

- You will continue to take your ART and any other medications that you normally take. If however, you are required to take antibiotics, you may be required to leave the study as this will affect the results in an unwanted way.
- There are no other lifestyle or dietary changes you need to make.
- Participants will be checked on by research staff on the sample collection days which happen every 2 weeks and with phone calls between the sample collection days. This will provide a chance for you to report any side effects to the research team. Participants will also be provided with the phone number of a research team member who can be contacted if there are any issues in between phone call and sample days. The research team member will report any issues to the study coordinator. They will then decide on the best way to solve the problem. This may require consultation with your HIV doctor.

5 Other relevant information about the research project

This study will be conducted in Bhubaneswar only. It will be conducted by researchers from the All India Institute of Medical Sciences-Bhubaneswar and Flinders University of South Australia. Up to 30 adults from Bhubaneswar will participate in the study.

6 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 to take part and later change your mind, you are free to withdraw from the project at any stage. If you do decide to take part, you will be given this PICF to sign and you will be given 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 routine treatment, your relationship with those treating you or your relationship with the Bhubaneswar ART clinic.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at the ART clinic. Other options are available; these include continuing your usual medication and care regimen for HIV and any other conditions you may have. A member of the research team will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include:

- A benefit to your body especially your intestines and the bacteria that live there. This will likely only last as long as you are eating the HAMS;
- A benefit to your HIV disease;
- Being provided with the study foods for 56 days;
- Contributing to the research about gut health, HIV and resistant starch.

There may be no clear benefit felt or noticed by you from your participation in this research.

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

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with a member of the research team. This team will also be looking out for side effects. There may be side effects that the researchers do not expect or do not know about yet. Tell a research team member or your HIV doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. This is very unlikely to occur after eating HAMS. If a severe side effect or reaction occurs, the research team may need to stop your participation in the study. The research team and your HIV doctor will discuss the best way of managing any side effects with you.

Possible side effects:

- flatulence, bloating, gas, increased frequency of passing stool, increased size and weight of stool.

If you experience these side effects they will almost certainly go away once you stop consuming the HAMS. If they cause you significant discomfort, you are free to stop your participation in the study.

The effects of high doses of HAMS on the unborn child and on the newborn baby are not known. Because HAMS has been certified with Generally Recognized as Safe (GRAS) status from the United States Government, it is very unlikely that it could harm the growing baby or mother. However, since eating large amounts of HAMS can change what happens in the gut normally, pregnant women should not participate in this study. Women who may be pregnant will be asked to do a simple pregnancy test with a small sample of their urine before they start the study.

Having a blood sample taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated. You should raise this with the research team if it becomes an issue. The blood sample will be taken in the same way as the ones you have for your normal HIV care at the clinic.

10 What will happen to my test samples?

The collection of your stool and blood will allow the researchers to test the effect of the HAMS on the health of your gut and if there is any effect on your HIV disease. The laboratory will use the following tests:

<u>Stool</u>

- pH (a measure of how acidic your stool sample is)
- short chain fatty acids (a measure of fermentation in your large intestine)
- the number and type of bacteria present in your large intestine
- calprotectin which measures if your gut is inflamed
- total, digestible and resistant starch (the different types of starch present in your stool).

<u>Blood</u>

- CD4+ T cell count (the measure of your immune response to HIV infection)
- HIV viral load (how much HIV is present)

The containers for your stool and blood samples will be labelled with only your participant identifier code to protect your confidentiality. The only researchers able to re-identify your samples from the code is by referring to the code key which will be kept in a password-protected document on a password protected computer by the study coordinator and Principal Investigator-India, Dr. Ramadass.

Any leftover supply of your blood and stool will be stored for future tests. Blood and stool samples will be stored at the AIIMS laboratory of the Principal Investigator-India, Dr Ramadass, to be used within the next 5 years for other tests to see how resistant starch changes your body. For example, blood samples may be used to test if the resistant starch made your gut wall stronger. Stool samples may be

used to test if resistant starch changed the bacteria that live in your gut. These extra tests can be done once the results of the first tests are known.

By providing consent, you are giving permission for the collection and analysis of your blood and stool and storage of any leftover samples for use in future studies even if they are not related to this study.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the research team will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, the research team will make arrangements for your regular health care to continue. If you decide to continue in the study, you will be asked to sign an updated consent form. Also, on receiving new information, the research team might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

There is no restriction on taking other treatment or medications during the study period other than antibiotics which will require you to withdraw from the study. Please discuss with the research team if you need to start a course of antibiotics.

13 What if I withdraw from this research project?

If you decide to withdraw from the study, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements about withdrawing. If you do withdraw your consent during the research project, the research team 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 law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

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

• Unacceptable side effects

15 What happens when the research project ends?

A summary report of the study results will be provided back to participants within 6 months of the completion of the laboratory analysis.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

Following your participation in the study, documents containing the results will be stored in a secure filing cabinet in the office of the study coordinator in Australia or on a password-protected computer in the case of soft copies. Study data will be stored away (‘archived’) 2 years after publication of the study results are published in a report. Summary data may be used in future reports or funding proposals. By signing the consent form you consent to the research team 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 provided to other people with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of checking the procedures and the data) by the relevant authorities and authorised representatives of Flinders University of South Australia, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

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 permission. Reporting will be about the whole group of participants together or by using participant's confidential identifier codes only.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Indian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team for this study. 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.

Any information obtained for the purpose of this research project and for the future research described in Section 16 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.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment.

18 Who is organising and funding the research?

This research project is being conducted by Ms Elissa Mortimer on behalf of Flinders University under the direction of Dr Balamurugan Ramadass from the All India Institute of Medical Sciences-Bhubaneswar.

Flinders University and All India Institute of Medical Sciences-Bhubaneswar may benefit financially from this research project if, for example, the project assists these institutions to obtain approval for a new therapy.

By taking part in this research project you agree that samples of your blood or stool (or results from analysing your blood or stool) may be provided to Flinders University or All India Institute of Medical Sciences-Bhubaneswar and that these institutions may directly or indirectly benefit financially from your samples or from what is learnt from analysis of your samples.

You will not benefit financially from your involvement in this research project even if, for example, your samples (or what is learnt from analysis of your samples) proves to be of commercial value to Flinders University or All India Institute of Medical Sciences-Bhubaneswar.

In addition, if what is learnt from this research leads to discoveries that are of commercial value to Flinders University or All India Institute of Medical Sciences-Bhubaneswar, the research team or their institutions, there will be no financial benefit to you or your family from these discoveries.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research administered from 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 Southern Adelaide Clinical Human Research Ethics Committee and the Institute Ethics Committee (IEC) of the All India Institute of Medical Sciences-Bhubaneswar.

This project will be carried out according to the Australian *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.

20 Further information and who to contact

The person you may need to contact will depend on what your question is about. If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact any of the following people:

Clinical contact person

Name	Dr Balamurugan Ramadass
Position	Assistant Professor
Telephone	(+91) 8547805341
Email	balaramadass1@gmail.com

Complaints contacts:

Name	Dr Balamurugan Ramadass
Position	Assistant Professor
Telephone	(+91) 8547805341
Email	balaramadass1@gmail.com

Name	Ms Elissa Mortimer
Position	Study Coordinator and Principal Investigator
Telephone	+61 415216907
Email	elissa.mortimer@flinders.edu.au

Name	Southern Adelaide Local Health Network
Position	Director, Office for Research
Telephone	8204 6453
Email	Health.SALHNOfficeforResearch@sa.gov.au

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	All India Institute of Medical Sciences (AIIMS)-Bhubaneswar IEC
HREC Executive Officer	Member Secretary, Arvind Kumar Singh
Telephone	(+91) 96549 05213
Email	arvind28aug@gmail.com

Consent Form - *Adult providing own consent*

Title	What is the effect of a dietary resistant starch intervention on the colonic luminal environment and HIV-related immunity and is a feeding trial feasible in HIV-positive adults in India?
Short Title	Resistant starch in HIV-positive adults in India.
Project Sponsor	Flinders University
Coordinating Principal Investigator/ Principal Investigator	Professor Paul Ward- Chief Investigator Assistant Professor Balamurugan Ramadass- Principal Investigator-India (PI-India) Ms. Elissa Mortimer-Study Coordinator and Principal Investigator.
Associate Investigator(s)	Professor Geraint Rogers Professor Graeme Young Professor BS Ramakrishna
Location of recruitment	Bhubaneswar, India

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 give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Flinders University of South Australia and All India Institute of Medical Sciences-Bhubaneswar, concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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 study without affecting my future health care.

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

Name of Participant (please print) _____

Signature _____ Date _____

Thumbprint

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

Signature _____ Date _____

† A senior member of the research team (Study Coordinator or Principal Investigator) must provide the explanation of, and information concerning, the research project.

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

I also consent to providing blood and stool samples and the storage and use of these samples, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Other research that is closely related to this research project
- Any future research.

Name of Participant (please print) _____

Signature _____ Date _____

Thumbprint

Name of Witness* to Participant's Signature (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 Senior Researcher†

Name of Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team (Study Coordinator or Principal Investigator) 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 - *Adult providing own consent*

Title	What is the effect of a dietary resistant starch intervention on the colonic luminal environment and HIV-related immunity and is a feeding trial feasible in HIV-positive adults in India?
Short Title	Resistant starch in HIV-positive adults in India.
Project Sponsor	Flinders University
Coordinating Principal Investigator/ Principal Investigator	Professor Paul Ward- Chief Investigator Assistant Professor Balamurugan Ramadass-Principal Investigator-India (PI-India) Ms. Elissa Mortimer-Study Coordinator and Principal Investigator
Associate Investigator(s)	Professor Geraint Rogers Professor Graeme Young Professor BS Ramakrishna
Location of recruitment	Bhubaneswar, India

Declaration by Participant

I wish to withdraw from participation 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 All India Institute of Medical Sciences-Bhubaneswar, ART Clinic Bhubaneswar or Flinders University of South Australia.

Name of Participant (please print) _____

Signature _____ Date _____

Thumbprint

Circumstances of withdrawal:

Declaration by 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 Senior Researcher†
(please print) _____

Signature _____ Date _____

† A senior member of the research team (Study Coordinator or Principal Investigator) 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.