PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Consent Form Version: Version 1.0
Consent Form Date: 18th Sept 2023

You are being invited to participate in a research study. Your participation in this study is entirely voluntary. Before you take part in this research study, the study must be explained to you and you will be given the chance to ask questions. Your questions will be answered clearly and to your satisfaction.

Please read the information provided here carefully. If you agree to participate, please sign the informed consent form. You will be given a copy of this document.

If you have any questions on this research study, please see the section below on:

WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY.

1 STUDY INFORMATION

Protocol Title:

Identifying **mo**lecular **d**eterminants of **i**n**f**ertilit**y** in men (**MODIFY**)

Principal Investigator's Contact Details

a. **Name: Candida Vaz**

b. **Department: Human Development**

c. **Institution: Singapore Institute for Clinical Sciences (SICS)**

d. **Contact number: 8854 6302**

2 PURPOSE OF THE RESEARCH STUDY

The purpose of this study is to understand the underlying mechanisms of infertility caused by unknown factors. We propose to identify the small non-coding RNA (sncRNA) biomarkers of infertility and advance towards developing a more accurate and robust approach for infertility diagnosis.

You are selected as a possible participant in this study because you are a male and aged between 21 to 50 years.

This study targets to recruit up to 100 men from local community outreach in Singapore over a period of 12 months.

3 STUDY PROCEDURES

If you agree to take part in this study, your participation in the study will last from when you are enrolled up till your semen collection is collected (e.g. within 1 week). The total duration of participation will be inclusive of 1 study visit (V1) and 1 home-based collection (for semen collection). You are required to attend one study visit at Human Development Research Center (HDRC), Singapore Institute for Clinical Sciences (SICS).

The study visit (V1) will last about one hour. At the study visit, informed consent will be taken, your height and weight measurements will be taken and you will be asked to fill a questionnaire. During the study visit you will be given a set of semen collection kit with instruction sheet (e.g on how to collect the semen sample at home with the semen container). On collection of your semen sample, you will inform the study team to arrange the courier service to collect the sample from your home.

All participants will undergo the same study procedures. You will be required to fast for at least 8 hours before collecting your semen sample. If you agree to take part in this study, the following samples ("human biological materials") / health information will be obtained:

Health Information (Questionnaire):
You will be asked to complete a questionnaire about your health and lifestyle related to the study. It will involve questions related to basic demographics, health conditions (age, ethnicity, BMI, education, disease conditions and treatments) and lifestyle (diet, supplements, frequency and duration of exercise, duration of sleep, smoking and alcohol consumption history, level of stress). It will take you approximately 10-15 minutes to complete the questionnaire).

Biological materials:

- **Semen samples:** You will need to provide a semen sample (minimum 1.5ml, about less than half a teaspoon) after 2-5 days of abstinence (refrain from intercourse or masturbation) and 8 hours of fasting for assessment of semen and sperm quality parameters (e.g. semen volume, sperm concentration, sperm count, sperm motility and vitality and for RNA extraction).

The HBM / health information will be analysed only in Singapore.

Schedule of Visits and Procedures:

You should follow the advice and directions given to you by the study team. Semen collection should be done using the semen collection kit and instruction sheet provided to you. You should collect your semen sample (minimum 1.5ml, about less than half a teaspoon) after 2-5 days of abstinence (refrain from intercourse or masturbation) and after fasting for at least 8 hours at home. You should then send the sample to us through the courier service that will be pre-arranged and booked for you. The semen sample submitted will be used specifically for research purposes after obtaining your consent.

The schedule of visits and procedures is outlined in the following table:

Study Visit (V1)	Recruitment, consent taking, height and weight measurement, and completing the health and lifestyle questionnaire. Time duration will be approximately 1 hour
Home-based collection (for semen collection)	Semen collection (collected using the semen collection kit with instruction sheet) You should collect your semen sample (minimum 1.5ml, about less than half a teaspoon) after at least 2 days of abstinence (refrain from intercourse or masturbation) and after fasting for at least 8 hours at home.

Restricted Research

The human biological materials collected will not be used in restricted human biomedical research involving human-animal combinations in accordance with the Human Biomedical Research Act 2015 of Singapore (HBRA).

Storage, Supply, Use or Export of Human Biological Material and/or Health Information

Any human biological materials and/or health information (de-identified) obtained during the course of this study will be stored and used only for the purposes of this study for a period not exceeding 15 years and will be thereafter destroyed.

Any human biological materials and/or health information containing your Personal Data that is collected for the purposes described in this Participant Information Sheet and Consent Form will be stored at SICS in Singapore. The human biological materials and/or data will be de-identified and transferred to our collaborators in other A*STAR RIs such as Genome Institute of Singapore (GIS) for research purposes. Our collaborators will take appropriate steps to ensure it complies with the data protection requirements in the Personal Data Protection Act while your Personal Data to be transferred remains in its possession or under its control.

To protect your identity, privacy and confidentiality, your human biological materials and/or stored data will be labelled with a code instead of information that directly identifies you (e.g. your name, NRIC, date of birth, etc.). We will keep a separate file (key) that links your code to your individually identifiable information. When we share your data and biological materials with other researchers, it will be in coded manner. They will not be able to identify you from the coded data and biological materials.

4 YOUR RESPONSIBILITIES IN THIS STUDY

If you agree to participate in this study, you should:

- Keep your study appointment. If it is necessary to miss the appointment, please contact the study staff to reschedule as soon as you know you will miss the appointment.

- Carefully follow the instructions provided in the instruction sheet for semen collection
- Follow the instructions provided by the study team
- Inform the study team if there is any issue related to semen collection

5 WHAT IS NOT STANDARD CARE OR EXPERIMENTAL IN THIS STUDY

The purpose of this study is to understand the molecular mechanisms of infertility and to discover infertility related biomarkers that have the capability of robust diagnosis. With further intensive research, these biomarkers can be developed into diagnostic kits and can help devise infertility treatment options. We hope that your participation will help us to investigate the biology of male infertility.

In this study, semen analyses can only be performed for the purposes of research and are not part of your routine medical care. Your semen sample will be used to assess semen and sperm quality parameters (e.g., semen volume, sperm concentration, sperm count, sperm motility and vitality). Besides this, small RNA will be extracted from sperm samples and sncRNA profiles will be obtained which will be compared (infertile vs fertile) to determine infertility related sncRNAs and their downstream targets. The semen sample collected will only be identified only by coded number and may be analyzed locally or abroad.

As a general assessment of your overall health, we will also collect some information through a health and lifestyle questionnaire solely for the purpose of research. This assessment of your health profile will be used to study its influence on these samples and their sncRNA profile.

6 POSSIBLE RISKS, DISCOMFORTS OR INCONVENIENCES

Personal privacy and confidentiality:
This study uses human biological material / health information that may affect your privacy. To protect your confidentiality, only a unique code number will be used to identify biological materials and/or health information that we collect from you.

As there will be a link between the code and your individually identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

Questionnaires
Some of the questions might make you feel uncomfortable or upset. Such discomfort is expected to be minimal. You may refuse to answer any of the questions and/or take a break at any time during the study.

Collection of semen samples:
Collection of semen may cause momentary inconveniences with no major risk or side effects. The collection of the semen sample is safe and non-invasive.

7 POTENTIAL BENEFITS

There is no direct benefit from participation in this study. However, you would be provided with a summary report on the quality profile of your semen and sperm sample. The report will help you track your fertility.

Moreover, your participation may add to the biological and medical knowledge that will help unravel the mechanisms of infertility, help in the development of diagnostic kits and novel therapeutic targets). Besides the scientific impact, this study will help raise societal and social awareness of pre-conception behaviour and its impact on fertility.

8 ALTERNATIVES TO PARTICIPATION

You can choose not to take part in this study. The study procedures will not be carried out.

9 COSTS & PAYMENTS FOR PARTICIPATING IN THIS STUDY

If you take part in this study, you will not be required to pay for any of the analysis. There are no expected costs to you for your participation in this study. There are no anticipated expenses related to sample collection. You will be reimbursed for your time, inconvenience and transportation costs as follows:

- For completion of Study visit 1 SGD $20 (for the completed questionnaire) worth of cash/vouchers
- For completion of home-based semen collection SGD $30 worth of cash/vouchers will be paid to you once your sample reaches us through the arranged courier service.
- You will be paid a total of SGD $50 worth of cash/vouchers for your participation in the study.

10 INCIDENTAL FINDINGS

During the course of the study, there is a possibility that we might unintentionally come to know of new information about your health condition from semen investigations that are conducted as part of the study. These are called “incidental findings”.

“Incidental findings” are findings that have potential health or reproductive importance to participants like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study. These findings may cause you to feel anxious and may affect your current or future life and/or health insurance coverage. Examples of potential incidental findings that may be discovered during the study may include but are not limited to fertility issues (from semen/sperm analysis). You will be asked to indicate whether you wish to be re-identified and notified in the event of an important incidental finding that is related to you.

If you agree to be re-identified and notified, the Principal Investigator will explain the incidental finding to you and discuss and advise you on the next steps to follow. You may wish to do more tests and seek advice to confirm this incidental finding. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

11 PARTICIPANT'S RIGHTS

Your participation in this study is entirely voluntary. Your questions will be answered clearly and to your satisfaction.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legally acceptable representative, if relevant) will be informed in a timely manner by the Principal Investigator or his / her representative and further consent may be required.

By signing and participating in the study, you do not waive any of your legal rights to revoke your consent and withdraw from the study at any time.

12 WITHDRAWAL FROM STUDY

Your decision to participate in this research is voluntary and completely up to you. You are free to withdraw your consent and discontinue your participation at any time without prejudice to you. Please inform the Principal Investigator if you decide to stop taking part in this study.

You are entitled to refuse to participate or discontinue participation at any time in this research.

If you withdraw from the study for any reason,

- Only your signed consent form and withdrawal form will be kept as a record.
- Such a withdrawal will prevent information about you from contributing to further research and analyses.

However, the data that have been collected until the time of your withdrawal will be kept and analysed. The reason is to enable a complete and comprehensive evaluation of the study.

The donation of any human biological material or provision of any health information is voluntary. The human biological material and / or health information collected for the study will be deemed to be given to Singapore Institute for Clinical Sciences (SICS) and will not be returned to you. You will also not have any right or claim to any share in the commercial gain derived from the research (if any) or intellectual property rights derived from the use of such human biological material and / or health information (if any). However, you retain your right to ask the Principal Investigator to discard or destroy any remaining samples if they have not beende-identified.

The Principal Investigator and / or the Sponsor of this study may stop your participation in the study at any time for one or more of the following reasons:

- Failure to follow the instructions of the Principal Investigator and / or study staff.
- You have certain health conditions and need treatment not allowed in the study.
- The study is cancelled.

13 RESEARCH RELATED INJURY AND COMPENSATION

If you follow the directions of the Principal Investigator and Study Team of this research study and you are injured due to the research procedure performed by the research study,

SICS will pay the medical expenses for the treatment of that injury.

Payment for management of the normally expected consequences of the procedures will not be provided by SICS.

SICS without legal commitment will compensate you for the injuries arising from your participation in the study without you having to prove SICS is at fault. There are however conditions and limitations to the extent of compensation provided. You may wish to discuss this with your Principal Investigator.

By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

14 CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS

Your participation in this study will involve the collection of Personal Data. "Personal Data" means data about you which makes you individually identifiable (i) from such data, or (ii) from that data and other information which an organisation has or likely to have access. Examples of personal data can include your name, national registration identity card (NRIC), nationality, passport information, date of birth and telephone number.

Personal Data collected for this study will be kept confidential. Your study records to the extent of the applicable laws and regulations, will not be made publicly available. Only the study team will have access to the personal data being collected from you. In the event of any publication regarding this study, your identity will remain confidential.

However, the Institutional Review Board, auditors and the regulatory authorities will be granted direct access to your study records to verify study procedures and data, without making any of your information public.

By signing the Consent Form, you consent to (i) the collection, access to, use and storage of your Personal Data by Singapore Institute for Clinical Sciences (SICS), and (ii) the disclosure of such Personal Data to our authorised service providers and relevant third parties as mentioned above.

By participating in this research study, you are confirming that you have read, understood and consent to the A*STAR Personal Data Protection Policy **(Annex A)**.

15 WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY

If you have questions about this research study or in the case of any injuries during the study, you may contact the Principal Investigator:

a. **Name: Dr Candida Vaz**

b. **Department: Human Development**

c. **Institution: Singapore Institute for Clinical Sciences (SICS)**

d. **Contact number: 8854 6302**

16 WHO HAS REVIEWED THE STUDY

This study has been reviewed by the A*STAR Institutional Review Board (IRB) for ethics approval.

If you have questions about your rights as a participant, you can contact the A*STAR IRB at hbro@hq.a-star.edu.sg.

Agency for Science, Technology and Research
SINGAPORE

Annex A

A*STAR's Personal Data Protection Brief

The A*STAR Personal Data Protection Brief sets out how the A*STAR GROUP (including the Research Institutes, centres, networks, consortia, subsidiaries and other units) collect, use or disclose Personal Data in compliance to the PDPA.

- **Consent, Purpose and Notification**
  A*STAR GROUP/ENTITY will notify individuals of the purposes for which their Personal Data is collected, used or disclosed by the A*STAR GROUP/ ENTITY and ensure that the individuals' consent have been obtained for such purposes.

- **Access and Correction**
  Individuals can make a written request to gain access, correct their Personal Data or withdraw consent to the processing of their Personal Data.

- **Accuracy**
  A*STAR GROUP/ENTITY will take reasonable efforts to ensures that Personal Data collected by or on behalf of the A*STAR GROUP/ ENTITY is accurate and complete.

- **Protection**
  Reasonable security arrangements will be put in place to protect Personal Data in the A*STAR GROUP's/ENTITY's possession or control from unauthorised access, collection, use, disclosure, copying, modifying, disposal or such similar risks.

- **Retention**
  Personal Data will be retained for as long as it is necessary to fulfill the purpose for which it is collected or for business or legal purposes, or in accordance with applicable laws.

- **Transfer Limitation**
  A*STAR GROUP/ENTITY will put in place agreements to regulate third party service providers outside Singapore to process Personal Data from A*STAR GROUP/ENTITY for administrative, business and/or legal purposes.

Queries in relation to A*STAR Personal Data Protection practices should be directed to our DPO at dpo@a-star.edu.sg .

CONSENT FORM FOR RESEARCH STUDY

Details of Research Study

Protocol Title:

Identifying **mo**lecular **d**eterminants of **i**n**f**ertili**y** in men (**MODIFY**)

Principal Investigator

a. **Name: Dr Candida Vaz**

b. **Department: Human Development**

c. **Institution: Singapore Institute for Clinical Sciences (SICS)**

d. **Contact number: 8854 6302**

Participant's Consent

I agree to participate in the research study as described and, on the terms, set out in the Participant Information Sheet.

The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I understand the purpose and procedures of this study. I have been given the Participant Information Sheet and the opportunity to ask questions about this study and am satisfied with the information provided to me.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without my medical care being affected.

By participating in this research study, I confirm that I have read, understood and consent to the A*STAR Personal Data Protection Policy.

Consent to be Re-identified and Notified in the case of an Incidental Finding

There may be potential incidental findings arising from this current research. Please indicate whether you consent to re-identification and notification about the incidental finding:

Please also check one of these boxes:

☐ Yes, I agree to be re-identified and I want to be contacted in the case of an incidental finding from this current research.

Phone:……..

Email: ……..

☐ In the event that I cannot be reached, please contact the following person nominated by me (optional):

Name:……

Phone: ……..

Email: ……

☐ No, I do not agree to be re-identified and I do not want to be contacted in the case of an incidental finding from this current research.

I understand that in rare situations where the incidental findings are life threatening or have public health implications and as required by the law (e.g. under the Infectious Diseases Act), I will be contacted and informed of the incidental findings even if I have indicated "No".

Name:……..

Phone:……

Email: ……

Consent for the Use of Human Biological Samples and/or Data for Future Research

Please indicate your options by indicating a tick (√) on the checkboxes:	Yes	No
Do you agree to donate your semen samples for future research as long as the research is related to fertility?	☐	☐
Do you consent for your data to be used for future research as long as the research is related to fertility?	☐	☐
Note: If you answer "Yes" to any of the above, please also indicate your consent for the following:		
Do you agree for the samples and data to be transferred outside of Singapore for future research?	☐	☐

Name of participant _____ Signature/Thumbprint (Right/Left) _____ Date of signing _____

To be completed by parent / legal guardian / legal representative, where applicable.

I hereby give consent for the above participant to participate in the proposed research study. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I confirm that I have read, understood and consent to the A*STAR Personal Data Protection Policy.

Name of participant's parent /legal guardian/ legal representative _____ Signature/Thumbprint (Right/Left) _____ Date of signing _____

To be completed by translator, if required.
(If the participant is unable to understand English and read any of the translated consent documents available.)

The study has been explained to the participant / the participant's legal representative in

_____ by _____.
Language Name of translator

To be completed by witness, where applicable.
(only for interventional, invasive and/or restricted research under HBRA)

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant or the participant's legal representative signing this informed consent form had the study fully explained to him / her in a language understood by him/her and clearly understands the nature, risks and benefits of his / her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date of signing

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant's legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant or legal representative thumbprint). After the written consent form and any written information to be provided to participant, is read and explained to the participant or the participant's legal representative, and after the participant or the participant's legal representative has orally consented to the participant's participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under HBRA (refer to HBRA, Part 3, Section 6(d) and HBR Regulations 2017, Part 4 Section 25 and 26).

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant's legal representative is able to read, sign and date on the consent form.

Investigator's Statement

I, the undersigned, certify to the best of my knowledge that the participant / participant's legal representative signing this consent form had the study fully explained and clearly understands the nature, risks and benefits of his / her participation in the study.

Name of Investigator / Person obtaining consent	Signature	Date of signing