RESEARCH CONSENT FORM

1. Title of research

Clinical Implementation of Pharmacogenetic Genotype-Guided Dosing of Warfarin in Patients With Heart Valve Replacement In Qatar

2. Principal Investigator

Dr. Amr Salah Omar, Sr Consultant Intensivist, Heart Hospital, HMC

3. Why are we inviting you to join this research?

The investigators at Hamad Medical Corporation (HMC) and Qatar Genome program (QGP) are conducting this research.

Heart patients undergoing heart valve replacement and eligible for warfarin treatment post-surgery will be invited to participate in the study. Investigators will study the role of the genome in the patient's response to warfarin therapy. This will lead to develop effective and appropriate dosing of warfarin tailored to the patient's genetic data.

4. What should you know about this research?

- Warfarin treatment is mandatory after cardiac surgery. Warfarin showed large interindividual variation that affects the dose required for a target therapeutic effect. The study aims to personalize warfarin therapy using genetic testing
- Eligible patients will be invited to participate in this study. Participation in the research project is voluntary. Patients have the right to enroll and/or refuse to participate in the study; and this will not affect the patients' medical care.
- Enrollment to the research study will not prevent the patients from receiving the clinical care and it will not affect the patients' therapeutic plan.
- Study participants have the right to withdraw from the study at any time without penalty or impact on the received clinical care.
- The purpose of this consent process is to give a comprehensive information about the study, so that a participant can decide about his/her enrollment in the study. Eligible participants must read this consent form carefully before taking the decision of their participation. Once the participants decide to take part in this study, they must sign this form. A copy of the signed consent will be given to the study participant.
- The information described in the consent form will be discussed with the participants by the research team. If participants have any questions or comments, they should ask their treating physician and/or the research team before making their decision.

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5. Who can you talk to?

Study participants are highly advised to contact the research team for at any time for the following reasons:

- Questions and/or concerns related to the project.
- Development of side effects or complications related to the study.
- Withdrawal from the project.

The research team focal person is:
Dr. Tamer M. M. Abdalghafoor
Cardiologist
Tel: +97450629799

Participants who have questions about their rights as volunteers, or want to talk to someone outside the research team must contact:

- HMC-IRB Office at 4025 6410 (from Sunday to Thursday between 7:00am-3:00pm) or email at irb@hamad.qa

6. Why are we doing the research?

Blood and tissue samples contain genes (DNA) that serve as the "instruction book" for the human body. The biological samples and the medical information will help the researchers to study how genes influence the response to medication.
The aim is to identify the genetic factors that predict the best response to warfarin therapy to enhance efficacy and decrease side effect.

7. How long will the research take?

The total estimated duration of the study is up to 3 years. You will be interviewed once by the research team to obtain consent. The research team will follow your treatment response and clinical progress during the treatment for 30 days after heart valve replacement.

8. How many people will take part?

The plan is to study patients who are enrolled to the department of cardiothoracic surgery (heart hospital) and referred for heart valve replacement. The targeted study size is 150 patients.

9. What happens if you take part?

If you agree to join, we will ask you to do the following:

- Provide a buccal swab for genetic testing
- Provide 3-4 ml blood sample for coagulation assessment based on a preidentified schedule.
- Attend your routine clinical follow up visits. If you are going for heart valve replacement you will adhere to clinical visit for 30 days post surgery.
- This study will help determine how genetic information is affecting your anticoagulant response. The whole procedure of genetic testing will take about 60 minutes.
- Clinical information and treatment data that are required for the purpose of the research will be collected during the study and during the follow up period.

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10. Could the research be bad for you?

- Minimum risk is associated with blood drawing. This includes discomforts when inserting the needle for the blood collection. There is a small chance that participants may develop a bruise or an infection at the needle site or feel lightheaded or faint.
- The research team will employ several methods to protect the participants identity and confidentiality. All identifiers will be saved in protected and encrypted files.
- The research team will ensure the security and privacy of participants data using encrypted and protected files. However, there is a very minimum risk of unauthorized access to and misuse of information, if there is a leak of any information or hacking to the system.
- Genetic information is highly sensitive, and the research team will implement the maximum-security measures to protect the participants' genetic data. There are a few approaches that link the genetic information back to the person's identifier. There are a number of potential risks with the advances of genomic research including; development of new methods to link the genetic material to the person's identifiers, risks to certain medical conditions that cannot be predicted at the time of conducting the research, and the results of the current research might be different in the future with more research outcomes related to the subject.
- The genetic information is unique to each person. However, individuals share some of the genetic information with their blood relatives. This genetic information could help to identify the individual who share the same genetic material. Also, the person's genetic information can be used to identify his/her relatives.
- Strict access to data will be implemented to protect participants information (see Section 12). However, people may develop ways in the future to link genetic or medical information in the research databases back to participant's identifier. For example, someone could compare information in the research databases with information from the participant (or a blood relative) in another database which may lead to the participants' identifier you (or the participant's blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking participant's genetic and medical information to participant's identifier.
- Since some genetic variations can help to predict future health problems, this information might be of interest to health providers, life insurance companies, and others. Law enforcement agencies can also use genetic variations to identify a person or his/her blood relatives. Therefore, participant's genetic information may be used in ways that cause a distress to the participant or his/her family members, such as revealing the risk to certain genetic diseases to the participant (or participant's blood relative).
- It is possible that study findings could one day help people of the same ethnicity or gender as the study participants. However, it is also possible that genetic traits might become associated with the study group and might reinforce harmful stereotypes.

11. Could the research be good for you?

- The possible benefits include knowing your genetic test results and personalizing your therapy to get maximum response with the least number of adverse effects based on your DNA. We hope the information we get from this study may help develop a greater understanding of genetic testing in the future.
- This kind of research usually takes a long time to produce medically useful results, so we will report genetic test to your doctor only and it may be linked to your electronic health record
- Your participation may, however, help patients in the future by improving the knowledge of response to drugs and improving medical care.

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12. What happens to information about you?

- The research team will ensure the security of all subjects' information. This includes de-identifying the participants using a coding system to identify the participants in the project records instead. The research team will not refer to participants' personal identifiers in any reports or publications out of this research.
- The research team cannot guarantee complete secrecy but will limit access to information about study participants. Only people who have a need to review information will have access. These people might include:
    - Members of the research team and representatives from other research group who work in a related topic or representatives from ethical committees who protect participants' rights and safety
    - Representatives of the Ministry of Public Health Qatar, HMC and QGP who make sure the study is done properly and that participants' rights and safety are protected
    - The treating physicians

- Few members of the research team will have access to the participants' identifiers to ensure the quality of the study. Those members will not share any personal identifiers with other research members and will keep all personal information confidential.
- Blood samples will be stored securely with coded numbers that do not include any personal identifying information. Information about participants' samples will be kept in a secure computer file that will be used by authorized team members.
- The results of this study will be discussed at scientific meetings and/or published in scientific journals.
- Personal identifiers of study subjects will not be used in any scientific meeting or written publication.
- Researchers from other groups may have access to data from the current study for analytical purposes. Request to access the data will be reviewed and approved through standard approval methods followed by HMC. All data will be anonymized and labelled with coded numbers. However, information such as dates of medical tests and services can be shared if requested without any link to personal identifiers.
- At the end of the study, all documents that include participants' name or other personal identifiers will be stored in a locked facility at QGP for at least 3 years. Only the study doctor or study research members who assist the doctor will have access to these documents. After five years, the documents will be destroyed.
- All blood samples collected for the research study will be considered as donations from the study participants. All personal identifiers that link the blood samples to the participants will not be used to label or identify the samples.
- The research team or the treating physician may inform the participants about the genetic variations identified in the study that may have an impact on the participants health if they are interested in receiving this information.
- The research team may request to integrate the clinical genetic test results in the electronic medical record.
- The research team may use information from the participants' electronic medical records to study the relationship between genetic makeup and health and disease.

13. What if you don't want to join?

- This study is voluntary. The participant has the right to refuse the participation to the research without penalty or consequences.

14. What if you join but change your mind?

- You can stop participating at any time and we will not hold it against you.

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- We will tell you about any new information that might affect your health or welfare, or might affect your willingness to continue in the research.
- If you stop early, please contact us. There is no safety or legal concerns about your decision If you stop participating, we will ask you for permission to keep the processed data in out records. Your donated sample will be destroyed and no further analysis will be done

15. What else should you know?

- This research is funded by QGP a member of QF.
- If an injury is caused as a direct result of research procedures, participants must contact the research team to receive the appropriate care available at HMC. If a participant seeks care outside HMC, the participant will be responsible to cover the cost of the received medical care. No compensation is available in case of injuries.
- The investigator or the research team may decide to stop the study or exclude some participants from the project at any time, even if those participants want to continue.
- No financial incentives will be offered for the study participants.

16. Additional Choices

We would like your permission to contact you about participating in future studies. You may still join this study even if you do not permit future contact. You may also change your mind about this choice. Please initial your choice below:

_____YES, you may contact me

_____NO, you may NOT contact me

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Signature Page for Capable Adult

Volunteer

I voluntarily agree to join the research described in this form.

Printed Name of Volunteer

Signature of Volunteer Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the volunteer.*
- *I have personally evaluated the volunteer's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the volunteer, who appears to have understood and freely given Consent to join the research.

Printed Name of Witness

Signature of Witness Date

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