MOH Health Research Proposal:

A1. Full title of the research: The full title should be consistent with that on any official documents used for regulatory purposes.

A2-1. Educational Projects:

- In most cases, it is expected that if projects are undertaken by a student in fulfilment of educational qualifications below graduate (Masters) level, the academic supervisor will take on the role of Principal Investigator. If acting as the Principal Investigator, the academic supervisor should sign both the Principal Investigator and supervisor declarations in **Part D**.
- It is normally expected that a doctoral student undertaking a project will be named as the Principal Investigator rather than the academic supervisor.
- A copy of a current CV of the applicant (the student[s] or the academic supervisor[s]) (maximum 2 pages of A4) must be submitted with the application.

A3. Principal Investigator:

- The principal investigator (PI) is the person designated as taking overall responsibility within a team of researchers for the design, conduct and reporting of the study.
- The named PI must be professionally based in Bahrain. For international studies with a PI or "Coordinating investigator" outside Bahrain, the form should name as PI the investigator who will take responsibility for the study within Bahrain.
- For research that is funded by a grant, the PI should normally be the grant-holder.
- For student projects (below graduate degree, Masters), the PI should be the academic supervisor
- For Master degree and PhD student projects, the student must be named as the PI.
- A CV for the PI should be submitted with the application. The CV should be in summary form, with only information relevant to the current application. For example, it should give evidence of previous research in the same field of study, and other relevant experience and training.

A4-2: Links with previous studies or other applications:

If this research is a follow-up study to a previous or current application by the Principal Investigator, or if the application is part of a series of closely-linked projects in a programme, give the details of relevant previous or current applications. This information will allow reviewers to access relevant background information if required. Please do not list all past and current applications unless directly relevant to this application.

1. Overview of the research:

- This section gives you the opportunity to summarize your project and the ethical and study design issues for your study.
- You may find there is some duplication with later questions, but the answers here will provide the RTST and other reviewers with an easy-to-read description of your study and the main issues. You may "cut and paste" information from this section for answers to later questions where appropriate.

A6. Writing a research summary (Abstract):

- Your answer to this question should be a short summary of the proposed research written in plain English. Where technical terms are used they should be explained. All acronyms should be described in full.
- The questions to cover in writing the summary:
    - **Why?** What research question is being addressed?
    - **What?** What research area (disease/ therapy/service) is being studied?
    - **Who?** Who will participate (inclusion/exclusion criteria)?
    - **Where?** Where is the study being conducted?
    - **How?** What are the procedures the patients/participants will undergo? How long is the study duration?

A10. Scientific justification of the research:

Should include:

- Background of the research problem
- Significance of the research problem
- What is the knowledge gap this research study is designed to fill?
- Has similar research on this topic been done before (in the Arab region and in Bahrain)?

Please support your statements with suitable references.

A11. Study design and methodology:

Depending on the type of research undertaken, the answer should include the following information:

- **Study design:** Type of study design, why the study design and methodology has been chosen.
- **Study area/setting:** Where will the study take place?
- **Study procedures:** What procedures the participants will undergo, how many times and in what order.
- The **broad timetable** for the stages of the research e.g. preparation, conducting interviews, interpreting and analysing findings, preparing the final report.

A15 & A16. Research procedures to be undertaken:

- These questions request detailed information about all the interventions and procedures that will be received by participants, or conducted on samples or data.
- The RTST will assess the risk and ethical acceptability of what is involved for potential participants. In particular it will wish to consider the nature and number of procedures compared to what a research participant might receive if undergoing treatment or other service provision alone.
- In column 1, give the **total** number of interventions or procedures, including routine procedures.
- If some of the interventions or procedures are regarded generally as routine care, give the number in the column 2.
- In column 3 give the average time taken to conduct each intervention or procedure. Some activities will overlap but the time for each should still be listed separately, e.g. an in-patient hospitalisation = 3 days and obtaining a blood sample lasting 10 minutes.
- In column 4 give either the name and job title of the individual conducting the research intervention or procedure (if it will always be the same person at all research sites), or give a description of the staff group, e.g. research nurse at site. Please also provide a general description of where the intervention/procedure will take place, e.g. out-patient clinic, GP practice or participant's home.
- Clinical interventions are those that are routinely conducted or requested by a healthcare professional.
- Information given about ionising radiation exposures (e.g. number of diagnostic X-rays, CT scans or courses of radiotherapy) should be consistent with the information provided in **Part B** of MOH RAS.

A17. Withdrawal of treatment or other services normally provided:

- Sometimes a research protocol requires withdrawal of existing treatment or service provision from the study subject. For example, it may be justified to stop current therapy during a "washout period". Researchers must ensure that treatment will be withdrawn only when absolutely necessary.
- You should explain the possible consequences of withdrawing treatment, and how you would minimise the possibility of any harm to the study subject.
- This should be reflected in the Participant Information Sheet as well.

A19. Potential risks and burdens:

- If the research only involves data collection, please describe any risks for patients associated with any breach of confidence or failure to maintain data security.
- These risks should be reflected in the Participant Information Sheet.

A20. Disclosure of information from interview/questionnaire:

- If interviews cover sensitive topics, the RTST members will review the experience of researchers and how they will handle these aspects.
- These risks should be reflected in the Participant Information Sheet as well.

A23-1. Identifying potential participants:

- If potential participants will be referred by an MOH department/health centre/hospital, the arrangements for identification and referral must be clearly described here.
- Details of the departments/ health centres/hospitals undertaking such referral of MOH patients must also be mentioned in **Part C**.
- Any publicity, letter of invitation and/ or written information for participants must clearly explain to the participant how they were identified.

A23-2. Screening of identifiable personal information

- Please give details of the sources of identifiable personal information that will be used to identify potential participants (e.g., disease registers, CIO data, medical records, etc.)
- If patient or disease registries are used to identify potential participants, give brief details of the consent and confidentiality arrangements of the registry.

A23-4. Access to personal data of patients by persons outside the healthcare team

- Normally, only the patients' existing doctors should have access to patient records without explicit consent to identify potential participants, check whether they meet the inclusion criteria or make the initial approach to patients.
- If the researcher (who is not the patients' doctor) will be identifying participants and making the first contact, the reason for this should be explained.
- The "direct healthcare team" are doctors who are directly responsible for providing routine care and treatment to individual patients together with their administrative support staff. Normally, such clinical staff will have direct contact with the patients. As pathology staff also directly support the care provided to patients they would also be included within the boundaries of the healthcare care team.

A23-5. Consent for access to identifiable personal data

- Consent must be explicit for secondary uses of identifiable data, such as for health research.
- Although past custom and practice has been that researchers have often been given access to records in order to identify relevant patients in order either to extract relevant data or to invite those patients to seek consent, this involves a breach of confidentiality.
- Therefore, consent should be sought by the clinical care team to allow researchers access to the records in order to extract information or to identify patients for the purpose of informing them about a research study, if the clinicians or their staff are unable to do this themselves.

A24. Research advertisements:

- The tone of the advertisements should be restrained. Care should be taken not to over-emphasize the benefits or make other inducements.
- State who will be the first point of contact for anyone who responds to the advertisement, and give brief details of their professional background and training for this task.

A23. Approaching participants:

- Participation in a research project must be entirely voluntary, and no one must be coerced to participate in a research project against his/her will. Researchers should avoid exerting undue influence when approaching potential participants. There should be no penalty if the participant decides to leave the research at any time.
- If the potential participant is a patient, the initial approach should normally be made by a member of the healthcare team. If researchers other than members of the healthcare team propose to approach potential participants directly, the reason for this approach should be explained.

A26-1. Informed consent:

For most types of research, it is both a legal and ethical requirement to obtain informed consent from participants who are able to consent for themselves.

Cases where informed consent is not required:

- Retrospective medical record review: If the investigator will not collect any patient identifiable information and no patient contact will be made.
- Collection of anonymised data: If the data to be collected has no personal information, e.g. anonymised data from disease registries, Health information directorate, CIO database, etc.

Vulnerable groups:

Participants who may feel induced or obligated to participate in the study. Vulnerable participants include:

- Unconscious patients
- Mentally ill patients

- Children
- Prisoners
- Participants known to the researcher (teacher-student, manager-employee, doctor-patient)

A26-2. Recording consent in writing:

- If you do not propose to obtain consent in writing you should justify this. The RTST usually requires that written consent be obtained for all procedures.'
- For studies involving postal or online questionnaires where sensitive topics are not involved, the return of the completed questionnaire by the participant can be regarded as adequate evidence of consent, and a written consent form is not required in this case. However, a participant information sheet explaining the study procedures is mandatory.
- If participants cannot sign the consent form, arrangements should be made for a witness to be present during the consent, and this should be documented.

A27. Research participants who may have difficulties in adequate understanding of English:

- The inclusion or exclusion of potential participants who do not understand written or verbal information in English raises ethical issues.
- If they are to be included, you should explain what measures will be taken to provide necessary translation of written information and interpretation. In a multi-site study, the PI is responsible for ensuring that all site investigators will make the necessary arrangements at each research site.
- Any proposal to exclude such participants should be clearly justified in the application.

A28. Providing new information during the study:

Participants should be aware of any new information that emerges during the research, which might affect their participation. You should describe your strategy for looking for, and disseminating, such information.

A29. Data processing activities:

Activities	*Guidance*
Access to medical records by those outside the direct healthcare team	This should only be undertaken with patient consent or MOH approval.
Electronic transfer by magnetic or optical media, email or computer networks	Where personal data is transferred electronically, data should be encrypted during transfer.
Sharing of personal data with other organizations	• Except when such disclosure has been allowed by participant consent or MOH approval, only anonymised data should be shared. • If data has been effectively pseudonymised, it should only be shared on the basis that the recipient cannot disclose the pseudonymised data to third parties and is not permitted to link the data with other data which might render the information more identifiable
Export of personal data outside Bahrain	• In general, patient level data should not be transferred outside Bahrain. This is because other countries do not have the same legal framework or protections for patient data. • Even if this is the case, it is difficult to manage and monitor the use of data to ensure it is safeguarded appropriately and is not misused.
Use of personal contact information (addresses, postcodes, faxes, emails, or telephone numbers)	It should be remembered that such personal contact details can be sensitive information, either because individuals are concerned about identity theft or because of domestic violence, etc.
Publication of direct quotations from respondents	Should be anonymised
Publication of data that might allow identification of individuals	In general, publication of patient case histories should be effectively anonymised. If identification is possible, it is essential that this is only undertaken with patient consent.

Storage of personal data on manual files (includes paper or film)	Paper and other manual files should be appropriately filed and stored in a secure location
Storage on MOH computers	Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to only those MOH employees who need access.
Storage on home or other personal computers	Patients' personal data or research participants' personal data should NOT be stored on a home or other personal computer, under any circumstances
Storage on University computers	Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to only those university faculty/students who need access.
Storage on Private company computers	Appropriate access controls need to be in place to ensure that access to confidential research information is restricted to only those employees who need access.
Laptop computers	Use of laptops and other portable devices is to be avoided. If it is necessary for them to be used, patient/participant data must be encrypted and the data uploaded onto a secure server or desktop as soon as possible. The data should be removed from the portable device as soon as possible using appropriate data destruction software.

A30. Physical security of storage:

- Explain if filing cabinets, cupboards and/ or rooms will be locked and who has access. Give details of security arrangements for personal data held on computers, especially where laptop computers are used.
- Information about security arrangements should not be extremely detailed to prevent access by anyone viewing this application.

A32. Access to participant's personal data during the study:

Monitors and auditors from pharmaceutical companies, research centres, and regulatory authorities may require access to the patients' clinical notes to verify or cross-check data.

The RTST is more likely to accept research protocols that incorporate such arrangements, provided that the following guidelines are observed:

- Participants should be informed in the Participant Information Sheet about who may have access to their medical records and research data, and why.
- Participants should have signed the consent form to state they have read the participant information sheet and understood the information it contains.

It may be appropriate to add that the participants' anonymised data may be used for preparation of a research report, and for submission to regulatory authorities.

A34. Retention of identifiable data:

- If valid participant consent is in place, identifiable personal data may be retained, but consideration should be given at the end of the study as to whether it is possible to reduce the identifiability of data.
- If data is to be processed without consent and only with approval from the MOH, the identifiability of the data must be reduced at the earliest reasonable point and the data must be anonymised/ pseudonymised effectively at the end of the study.

A37. Payments to research participants:

Payments and benefits

- Payment of participants should be ethically justified. The RTST wants to be reassured that the research participants are not being paid for taking risks or that the payments will not unduly influence participants.
- Information on any payments or benefits must be included in the Participant Information Sheet.
- If proposing payments, you should consider the possibility of non-cash payments, particularly for children.
- If you decide to introduce payments after receiving a favourable opinion from the RTST, these must be notified to the RTST as a substantial amendment and must be reviewed before being implemented.

Reimbursement of expenses

- Research participants should not have to spend substantially out of their own pocket during their participation.
- Payment in cash or kind to the participants must ONLY be for costs such as travel expenses, child-care expenses, meals and demonstrable loss of earnings, etc.

If it is not possible to reimburse such expenses, this should be explained before the research participant is recruited. A clear statement on reimbursements should be included in the Participant Information Sheet.

A38. Payment to researchers:

- This question is concerned with "in-pocket" financial payments or additional benefits provided to researchers personally, over and above the costs of conducting the research.
- Such payments could include, for example, contributions to a library, additional equipment not actually required for the research, social events, etc. The question is not concerned with payments agreed between the sponsor and MOH health centres or other sites to reimburse the costs of hosting the research.
- Personal payments or benefits to researchers should cause undue influence to participate.
- You should record the fact that researchers are receiving personal payments or benefits in the Participant Information Sheet

A40-1. General Practitioner:

- In the case of observational research, it is a matter of judgment as to whether the GPs or other doctors should be informed about their patient's participation in the research study.
- Researchers should consider whether study participation could have implications for healthcare by other doctors. It is possible that participants may approach them for advice about any aspect of the study. If so, it may be helpful for the GP/doctor to be aware of their patient's involvement. Advice on this may be sought from the RTST.

A40-2. Permission to notify the GP:

- The research participant should be advised in the Participant Information Sheet that his/her GP/health professional will be approached.

A41. Study registration:

- ICMJE endorses prospective registration of observational (clinical and non-clinical) health studies involving data collection from human participants.
- The following article provides sufficient rationale for registration of these studies: "Registration of observational studies: Is it time?"
- Observational studies can be registered on existing clinical trial registries like Clinicaltrials.gov and some registries linked to WHO's ICRTP network.
- In general, registration is not expected for projects undertaken entirely for educational purposes below graduate level.

A42. Distribution of study results and publication:

- The results of research should be reported, whether through publication in peer reviewed journals or other means of dissemination. Negative as well as positive results should be published, or at least made publicly available.
- Consideration should be given to providing feedback on the results to research participants, interested groups and communities (see **Question A46**).

A43. Ensuring anonymity of identifiable data in publications:

- Care should be taken when considering publishing data or case histories to ensure the anonymity of the relevant patients.
- For example, if tables of data are to be published, care should be taken where the values of cells are small numbers. This is because, in combination with other information, this could render information potentially identifiable.
- In relation to case histories, care should be taken that the combination of incidental details, e.g., details about occupation, location, age, and ethnicity do not lead to individuals being identified.

A44. Informing participants of the results:

- It is good practice to disseminate the results of research to research participants and other interested groups or communities. This provides feedback to the participants on the outcome of research towards which they have contributed.
- Consideration should be given to providing a summary sheet of the findings or letting participants know where they can access the results.
- In addition, it may be important to inform patient groups or communities of any findings that are relevant to their future healthcare.
- Information about publication arrangements should be included in the Participant Information Sheet.

A45. Primary endpoint:

- In quantitative research, the primary endpoint is a statement expressing how, in numerical terms, the primary objective of the study will be met from the data collected.
- For example, in a study of hypertension, the primary endpoint might be the systolic blood pressure at the final visit.
- There should normally be only one primary endpoint, though there may be more.

A46. Secondary endpoint:

Secondary endpoints are statements expressing how, in numerical terms, the secondary objectives of the study will be met from the data collected.

A47. Sample size:

- The sample for the research may include "participants" who are not approached in person, but whose records or samples will be studied.
- The number of participants should be sufficient to achieve worthwhile results but should not be so high as to involve unnecessary recruitment and burdens for participants.
- In the case of qualitative research, it is recognized that the number of participants may be small and will not be determined using a statistical power calculation. However, reviewers will find it helpful to know who you are targeting and why you are targeting them.

A49. Randomisation:

It is helpful to give the intended mechanism of randomisation, for example a sequence of opaque envelopes, or telephone or internet randomisation. It should be evident to reviewers that the concept of random allocation has been correctly understood, and will be seen to be free from bias.

A50. Methods of analysis:

- For studies with a quantitative (numerical) endpoint, give details of the methods that will be used to obtain the results for the primary and secondary endpoints, including the methods for summarizing the data with numbers or graphs, and the main statistical tests to be used where comparisons are to be made.
- Describe how you will handle missing data, for example due to withdrawal of participants or non-compliance.

For studies using qualitative methods, researchers should:

- Outline in simple terms exactly how the study data will be managed and analyzed.
- For example, will it be arranged into themes? If so, will this be done by use of a qualitative data analysis tool, by manual analysis and coding of the data, or by some other means? State why this is your chosen method of analysis.
- Give a brief description of any techniques to be used (e.g. framework, content or thematic analysis) for the benefit of lay members. Refer to any qualitative data software to be used.

A52. Research sponsor:

- The sponsor is the individual, company, institution or organisation, which takes on ultimate responsibility for that research.
- The sponsor takes primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting.
- Any research requiring the collaboration of the MOH must have an individual or organisation willing to take on the responsibilities of the research sponsor.
- Any research outside the MOH should also have a sponsor to take on the specific responsibilities of the role.
- The sponsor is usually, but does not have to be, the main funder of the research. It can also, for example, be the employer of the Principal Investigator, the educational institution, or the health centre/hospital where the research is to take place.

Sponsor's representative:

- It is possible that the duties of the sponsor could be shared between more than one party. If this applies, please enter as the "lead sponsor" in **A55-1** the one nominated to receive copies of correspondence from the RTST for this study. Enter further details of the co-sponsors in **A55-1**.
- An authorised representative of the lead sponsor should complete the sponsor declaration in Part D of IRAS. The person making this declaration does not necessarily have to be an employee of the sponsor, but should be authorised to do so by the sponsor. For example, a Contract Research Organisation (CRO) may be given delegated authority by the sponsor to prepare and submit applications for approval on their behalf.

A53. Funding:

- The information required here is the funding of the project costs of the researcher (which might include a contribution to salaries, other costs of research staff time, additional equipment and reagents, IT costs, administrative expenses, etc.). It does not include any funding agreed with the sponsor through a research contract to pay for the costs of hosting the research.

- Researchers are strongly advised to secure any project funding required from bodies outside the MOH before submitting the application for ethical review. If funding has not been secured, and the funding body later requires changes to be made to the proposal, these would require further review by the RTST. If the changes were major, the RTST would require submission of a new application.
- MOH staff researchers applying for MOH research funding must refer to the MOH Health Research Structure and Procedures before applying.

A54. Subcontractors:

- The sponsor retains the ultimate accountability for the research. However, if responsibility for any aspects of the research has been delegated to a subcontractor such as a Contract Research Organisation or Site Management Organisation, the RTST will wish to know this and you should make clear the extent of the delegated responsibility.
- Give the name of the organisation, including the name of a contact person within it. This should be the person the RTST can contact in case of queries

A55. Previous rejection of the research by a Research committee:

- If the research has been rejected previously, the RTST will wish to see a copy of the unfavourable opinion letter.
- You should also provide a covering letter explaining how the issues of concern have been addressed in this application.
- It does not necessarily mean that rejection in another country will result in rejection in Bahrain.

Part B: Section 1: Ionizing Radiation

2. Details of radioactive materials:

Please provide full information about each radioactive material being used. If more than one radionuclide is administered, generate a separate table for each radionuclide.

Notes on the table:

- Investigation: the investigation employing radioactive materials which is included in the study protocol.
- Radionuclide: the material which will be used.
- Proposed activity: the quantity which will be used in an individual investigation expressed in Microbecquerels (MBq).
- Route: the route by which the material will be given, e.g. intravenous, oral.
- Number of administrations: the number of individual investigations specified by the protocol for each study participant.

The information should match the information about these investigations included in Question 15 of **Part A of IRAS** ("Details of clinical interventions and procedures").

10. Assessment of additional exposure:

In undertaking the assessment, the lead CRE should consider:

- The specific objectives of the exposure and the characteristics of the research population
- The characteristics of the research population will include such factors as the age of the participants and their likely life expectancy.
- The potential diagnostic or therapeutic benefits, including direct benefits to the participant and the benefits to society
- The potential diagnostic or therapeutic benefits, including direct benefits to the participant and the benefits to society
- The Risk to participants that the exposure may cause
- The availability of alternative techniques involving less, or no, exposure to ionising radiation
- The possibility that participants will be participating in other trials involving additional radiation (Refer to **questions 12 and 26 in Part A of MOH RAS** for the selection criteria and details of possible involvement in other research.)

Part B: Section 2: Existing samples

1. Type of human tissue or other biological material:

Describe the body sites from where the samples will be collected, and the form in which the samples will be supplied. Indicate if the samples are perishable in nature, their likely deterioration time and the purposes for which they will be used.

2. Anonymisation of samples:

Samples from donors should normally not be identifiable to the researcher. This can be done if obvious identifiers (e.g. name, address, date of birth) are removed at the time of collection.

3-1. Consent:

It is best practice to seek consent for use in research wherever possible.

For historical tissue samples:

- If consent was previously obtained for use of the samples in research, please enclose a copy of the information sheet and consent form used.
- If consent was not obtained for use in research, researchers must consider whether it would be ethically appropriate and feasible to re-contact the donors. If you do not propose to do this, please justify.
- Details of how the donors will be identified and approached should be given in answer to **Questions A21 and A23**. A copy of the Participant information sheet and consent form should be enclosed.

5. Analysis or use of genetic material:

Answer "Yes" to this question if the analyses may produce information that involves genetic sequence data, single nucleotide polymorphism data, genetic "finger print" data, ploidy data or cytogenetic data, including the detection of mutations or genetic variants.

6-1. Clinically significant results:

- Indicate whether the analyses described in Question 6 could have prognostic, predictive or other significance for individual donors/subjects or their relatives.
- If so, describe the nature of the clinical significance for the individual subjects that might be encountered

6-2. Arrangements to notify individuals of clinically significant results:

- If "Yes", describe how the results will be provided. Will it be given directly to the participant or by a healthcare professional? In either case, please explain how the implications of the feedback will be explained to the participants and how they will be supported or counselled in light of the feedback.
- If some participants have indicated that they do not wish to receive clinically significant results, how will you deal with this in the light of clinically significant information resulting from the research?
- If No, indicate clearly the reasons why data will not be notified to the participants or their healthcare professionals.

9. Storage of samples:

- The RTST will wish to know where the samples will be stored during the project and where the tests and analysis will take place.
- Describe the arrangements for preserving the condition of the samples and for ensuring security and confidentiality of the samples and any linked data.
- Say who will be responsible for these arrangements and who will have access to the samples.

10. Further storage or disposal of samples at the end of the project:

- Ethical approval for storage of the samples will be confined to the specific project described in this application form and the protocol.
- This project-specific application form may not be used to seek open-ended approval for use of stored tissue in future research programmes. It is also not permitted to submit substantial amendments to approved projects in order to use tissue for another project with a different set of research questions.
- For plans to store the tissue beyond the life of the project for use in further projects, the researcher may make a further project-based application. The application must be submitted no later than the date on which the first project ends (as defined in the protocol).

Part B: Section 3: New samples

1. Type of human tissue or other biological material:

Describe the body sites from where the samples will be collected, and the form in which the samples will be supplied. Indicate if the samples are perishable in nature, their likely deterioration time and the purposes for which they will be used.

2. Collection of samples:

Briefly describe the arrangements for collecting the samples, mentioning any involvement of other collaborators. If the samples will be collected from a number of study centres, indicate the type of health care professional who will be involved. You may cross-refer to information already provided in Part A of the form.

3-2. Informed consent:

- If samples are collected primarily for research purposes, informed consent is **always** required to remove, store and use the tissue.
- If samples are collected from the living donors primarily for diagnostic or therapeutic purposes (e.g. for a blood test or biopsy, or in the course of surgery), it is best practice to seek consent prospectively for use in research where possible. Consent for use in research may be added to the established consent procedure for routine diagnosis or surgical treatment.
- If consent will not be sought for research, this should be ethically justified in your answer to Question A24-1.
- If consent will be sought, the answers to Questions A23 and A24-1 should describe how donors will be approached and who will undertake the consent process. The information sheet and consent form should be enclosed.
- The informed consent process should also deal with:
    - Confidentiality of personal data
- Whether donors would be able to withdraw consent and what the effect of this would be on their samples or data

3-3. Samples from the deceased:

- "Appropriate consent" is required to store or use tissue obtained from the deceased, unless the person died more than 100 years ago. Appropriate consent should be sought if not already been obtained for use in future research.
- In the case of a deceased adult, appropriate consent means:
    - The consent of the deceased person given before death.
    - If there is no prior consent by the deceased person, the consent of a legally acceptable representative nominated by the deceased.
    - If no representative was appointed by the deceased person, a person in a **qualifying relationship** (see below).
- In the case of a deceased child, appropriate consent means:
    - A person who had parental responsibility immediately before the child's death.
    - If no person had parental responsibility, another person in a **qualifying relationship**.

Qualifying relationship

- Persons in a qualifying relationship are ranked in the following order:
  (1) Spouse or partner (including civil partners);
  (2) Parent or child;
  (3) Brother or sister;
  (4) Grandparent or grandchild;
  (5) Child of a brother or sister;
  (6) Stepfather or stepmother;
  (7) Step brother or step sister;
  (8) Long-time friend.
- If there is more than one person in the same rank in the hierarchy, the consent of any one of them will constitute appropriate consent.

4. Anonymisation of samples:

Samples from donors should normally not be identifiable to the researcher. This can be done if obvious identifiers (e.g. name, address, date of birth) are removed at the time of collection.

6. Analysis of use of genetic material:

Answer "Yes" to this question if the analyses may produce information that involves genetic sequence data, single nucleotide polymorphism data, genetic "finger print" data, ploidy data or cytogenetic data, including the detection of mutations or genetic variants.

7-1. Clinically significant results:

- Indicate whether the analyses described in question 8 could have prognostic, predictive or other significance for individual donors/subjects or their relatives.
- If so, describe the nature of the clinical significance for the individual subjects that might be encountered

7-2. Arrangements to notify individuals of clinically significant results:

- If "Yes", describe how the results will be provided. Will it be given directly to the participant or by a healthcare professional? In either case, please explain how the implications of the feedback will be explained to the participants and how they will be supported or counselled in light of the feedback.
- If some participants have indicated that they do not wish to receive clinically significant results, how will you deal with this in the light of clinically significant information resulting from the research?
- If No, indicate clearly the reasons why data will not be notified to the participants or their healthcare professionals.

8. Storage of samples:

- The RTST will wish to know where the samples will be stored during the project and where the tests and analysis will take place.
- Describe the arrangements for preserving the condition of the samples and for ensuring security and confidentiality of the samples and any linked data.
- Say who will be responsible for these arrangements and who will have access to the samples.

9. Further storage or disposal of samples at the end of the study:

- Ethical approval for storage of the samples will be confined to the specific project described in this application form and the protocol.
- This project-specific application form may not be used to seek open-ended approval for use of stored tissue in future research programmes. It is also not permitted to submit substantial amendments to approved projects in order to use tissue for another project with a different set of research questions.
- For plans to store the tissue beyond the life of the project for use in further projects, the researcher may make a further project-based application. The application must be submitted no later than the date on which the first project ends (as defined in the protocol).

Part B: Section 4: Adults unable to consent

11. Loss of capacity to consent:

- It is necessary for researchers to consider what steps they would take in the event of a participant losing capacity to consent during the project.
- Researchers are not obliged to monitor the capacity of participants proactively during the study. However, they should be ready to address the consequences of a loss of capacity should this come to their attention at any point.

Option 3: Participant remains in the research study

- This option may apply where research participants are suffering from an impairing condition and their capacity to consent is borderline or fluctuating.

- Continued research on participants following loss of capacity would only be approved by the REC if the research met in full the criteria for including such participants in research, i.e. the nature of the research is such that it would have been justified to include participants lacking capacity from the outset.

Part C: Research sites:

- Please list all research sites and any local Site Investigators you plan to include in the research. Include any sites you plan to include later. It does not matter if agreement has not yet been reached with the site.
- Research sites are organizations responsible for participant-related research procedures specified in the protocol - including recruitment and informed consent. Referral of a patient for assessment and possible recruitment is not part of the conduct of the study. The following are not considered to be research sites:
    - Clinicians or clinical units making referrals to the research team.
    - Research units undertaking support functions, e.g. project management, site monitoring, data analysis or report writing.
- The research site is not necessarily the location where research activities will actually take place. For example, for a research project by nurses from a secondary care hospital, interviews with the participants may take place in the participant's home, but the research site would be the GP practice. If the research will be conducted at more than one location within the same site (for example, if the departments or clinics involved belong to a single hospital), this should normally be considered as a single site.
- Organizations' where clinicians refer potential participants to the research team for assessment and possible recruitment are not considered to be research sites. For example, a GP may identify potential participants, provide patients with information about a study and seek consent to pass on the patients' contact details to the research team. If the patients are then followed up by the research team and consent is subsequently obtained by the research team, the GP practice is not a research site, it is a Participant Identification Centre. See below for how to provide details about such organizations.
- In some cases, there may not be a local Site Investigator (part of the research team) for the site. In this situation you must identify a Local Collaborator at the site. The Local Collaborator will normally be the head of the department where the research will take place, e.g. Head of Physiotherapy for research involving questionnaires to physiotherapy staff.
- Non-MOH research sites may have individual arrangements for giving permission for research.

2. Research locations:

- The information supplied in this question should be in sufficient detail to allow the location(s) and scale of the research to be assessed. Explain which parts of the research will take place in each location, and give details of any major equipment or facilities that will be used.
- If facilities or equipment at a different location from the site are used, but the participants remain under the responsibility of the main site, then the details of protocol procedures conducted at other locations should be described here for that particular research site.

3. Number of participants:

Give details of the planned number of participants at each MOH site. The sample size for the research may include "participants" who are not approached but whose records or samples are to be studied.

Part D: Declarations

Declaration by Principal Investigator:

- Please read the bullet points carefully. By signing the declaration the Principal Investigator is legally agreeing to its contents and will be personally liable for any deviation from this agreement.
- Before proceeding to submit the MOH RAS application forms, please make sure you have correctly answered all questions in the Project Filter and all relevant sections and questions have been enabled and completed.
- Please ensure that all other relevant declarations in Part D are completed.
- Electronic authorization is available as an alternative to ink signature for most signatures required in MOH RAS.
- If an ink signature is provided, you are advised to scan and save an electronic file of the signed page and to retain a copy of the signed application.

Declaration by Sponsor's Representative:

- The sponsor's declaration confirms an agreement in principle by the organisation(s) named in the application to act as sponsor(s) for the study.
- Final confirmation of sponsorship arrangements must be in place before the study starts.
- The person signing the declaration should be authorised by the sponsor organization to do so.

Declaration by Academic supervisor:

- This declaration should be completed by the academic supervisor for all student applications.
- Academic supervisors should note that tasks under the responsibility of the academic supervisor may be delegated to a clinical supervisor at the MOH site where research activity is undertaken. Any such arrangement with a clinical supervisor should be agreed with the MOH site.