Kingdom of Bahrain
Ministry of Health

GUIDANCE TO APPLICANTS FOR THE APPROVAL OF HEALTH RESEARCH IN HUMAN SUBJECTS

Health Research Committee
2016

TABLE OF CONTENTS

PAGE

LIST OF FIGURES

PAGE

LIST OF APPENDICES

PAGE

LIST OF FORMS

PAGE

LIST OF ABBREVIATIONS

CRO	Contract Research Organization
EMA	European Medicines Agency
FDA	Food and Drug Administration, United States
ICF	Informed consent form
ICH	International Conference on Harmonization
GCP	Good Clinical Practice
HRC	Health Research Committee
MOH	Ministry of Health
NOC	No-Objection Certificate
PHCRC	Primary Health Care Research Sub-Committee
REB	Research Ethics Board
RTST	Research Technical Support Team
SHCRC	Secondary Health Care Research Sub-Committee

GLOSSARY OF TERMS

Adverse event:	An adverse event is any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product or research procedure. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.
Case Report Form:	A printed or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each research participant.
Good Clinical Practice:	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of research subjects are protected (*a guideline developed by the ICH).*
Greater than minimal risk research:	Research procedures that may include risk beyond that ordinarily encountered by participants. This research requires full review by the research committee.
Informed consent:	ICH GCP defines informed consent as a process by which a subject voluntarily confirms his or her willingness to participate in a particular research study, after having been informed of all aspects of the research that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.
Informed assent:	"Assent" is a term used to express willingness to participate in research by persons who are by definition too young to give informed consent but who are old enough to understand the proposed research in general, its expected risks and possible benefits, and the activities expected of them as subjects. Assent by itself, however, is not sufficient. If assent is given, informed consent must still be obtained from the subject's parents or guardian.

Informed consent form:	Signed approval form by which the subject confirms his or her willingness to participate in a particular research study.
Investigational product:	A form of an active ingredient being tested in a research study, including a marketed product when used in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Investigator's brochure:	A compilation of the clinical and non-clinical data on an investigational product(s), which is relevant to the study of investigational product(s) in human subjects. This document is usually submitted for Research approval in cases of clinical trials involving the use of an unapproved product/device.
Low-risk / Minimal risk:	Research in which the only foreseeable risk to the participant is one of discomfort.
Participant recruitment material:	This includes any type of communication (e.g. flyer, radio/television script, poster, newspaper advertisement, Internet message) that is directed to potential subjects for the purpose of recruitment. The purpose of submitting this documentation is to ensure that recruitment messages are appropriate and not coercive.
Protocol:	A document that describes the brief literature review, background, rationale, objective(s), design, methodology, statistical considerations and organization of a study.
Product monograph:	A factual, scientific document on a product that, devoid of promotional material, describes the properties, claims, indications, and conditions of use for the product, and that contains any other information that may be required for optimal, safe, and effective use of the product. This document is usually submitted for Research approval in cases of research studies involving the use of a marketed and licensed product/device.

INTRODUCTION

Health research, whether data obtained by questionnaires, or by means of a physical intervention on patients or health volunteers, seeks to diminish existing uncertainties and improve our understanding of health and disease. Ultimately, the results obtained in such research contribute to appropriate and improved healthcare directed at meeting patients' needs.

The Ministry of Health, Bahrain (MOH) wishes to encourage research related to fundamental biological processes, diseases of national priority and quality of healthcare management, in the belief that a collaborative research effort can accelerate the acquisition of knowledge more effectively than a simple aggregate of research projects that have no interaction or thematic integration. These projects are also viewed as an effective instrument in capacity building of a cadre of scientists and clinicians of the highest calibre.

The Health Research Committee (HRC) at the MOH plays a central role in the research process. As well as upholding the rights of research participants, the HRC is tasked with assessing the risk-benefit profile and methodology of research, ensuring consent is valid, protecting confidentiality and privacy of subjects, providing research grants and more recently with the monitoring of ongoing research. The scientific and ethical evaluation of a research protocol is not to be considered as an administrative obstacle but rather as an integral part of the research process.

This Guidance manual accompanies the *Online MOH Research Application System* developed for the approval of health-related research studies conducted within MOH healthcare facilities. It is a reference document that provides detailed context for the questions asked and directs applicants to other related sources of information.

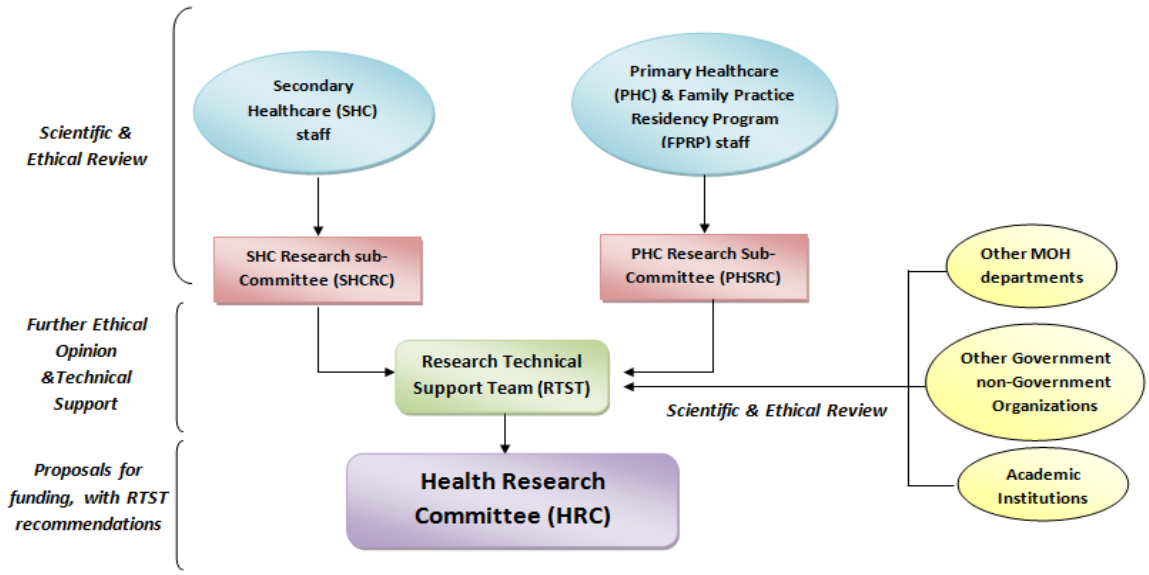
Undoubtedly, this document will significantly contribute to a more streamlined approach that should facilitate efficient ethical review of health research studies, and should improve the calibre of applications completed by researchers and submitted to the HRC. It will also be key in facilitating communication and interaction between researchers and the HRC, allowing both to work together as partners in the process of ethical review. It is therefore, strongly suggested that interested researchers consult the following instructions for proposed health research.

BACKGROUND: THE HEALTH RESEARCH STRUCTURE IN THE MINISTRY OF HEALTH

Health research was identified as one of the twelve strategic goals in the "Bahrain Health Strategy: Framework for Action 2015-2018" under the Strategic Goal No. 2:Integration of services in the Health system throughout Ministry of Health and with other governmental and private institutes , initiative No. 2: Develop Health Research Management System and link it with concerned stakeholders

Recognizing the importance of institutionalizing health research in the country, and in an effort to devote more resources towards establishing centres of excellence in biomedical research, the MOH set up a central Health Research Committee (HRC) in 2005 by Ministerial Order No. (19) based on which, a Research Technical Support Team (RTST) and three sub-committees; Primary Healthcare Research Sub-Committee (PHCRC), Secondary Health Care Research Sub-Committee (SHCRC) and College of Health Sciences Research Sub-Committee (CHSRC), were established. The aim of the RTST is to ensure that high ethical standards are maintained in research projects to protect the interests of research participants, investigators and the MOH.

Figure 1 Health Research Structure, MOH



INSTRUCTIONS FOR THE ETHICAL APPROVAL OF HEALTH RESEARCH

This guidance details the procedure for application to the RTST and the peripheral research sub-committees. For ease, the general term *'MOH Research Committee'* has been applied to refer to the above mentioned committees throughout the document.

1. GENERAL

a. Health-related research may be conducted within MOH hospitals/health centres **only** after official approval has been sought and obtained from an MOH Research Committee.

b. To ensure that the participants in research studies are not unduly exposed to unreasonable or unnecessary research risks, researchers must confirm that they have read the "MOH Ethical Guidelines for Health Research", the Declaration of Helsinki, and Good Clinical Practice (GCP), and ensure that their research is compliant with these guidelines.

c. The '*applicant'* for review and approval of a research project must be the Principal Investigator of the study (a student/ staff who is professionally based in Bahrain). The **MOH Online Research Application System** is accessible via the MOH intranet and internet websites.

d. Completing the application in accordance with the following recommended guidelines will speed up the process of approval and minimize any delays that could otherwise occur. Applicants can use the **Documentation Checklists** (Appendix B) for help with the completion and collation of the requisite supporting documents.

e. Only an application that satisfies all of the necessary information and documentation will be considered a '**complete**' application and will be scheduled for a **review**. Incorrect or incomplete applications will not be reviewed until all corrections / necessary documents are in place.

f. Researchers must conduct a *feasibility assessment* of the proposed sites for carrying out their research, **ahead of** submitting an application to the MOH Research Committees – to ensure that the facilities/departments can spare the required staff, supplies or equipment required.

g. **Approval from an MOH Research Committee does not automatically imply that the researcher is granted access to data, medical records or biological samples from MOH healthcare facilities.** Researchers must seek permission and follow procedures as dictated by the concerned departments after presenting them with a valid MOH approval letter.

2. RISK ASSESSMENT OF RESEARCH

Ethical approval should be considered for any research which involves human beings. Such studies may be of either a quantitative or qualitative nature. Currently, the MOH Research Committees reviews applications of all forms; however, the type of review depends on the type of research study, i.e., observational or interventional.

Please consider the following information to determine which category your research belongs to:

OBSERVATIONAL STUDIES (Non-interventional)	CLINICAL RESEARCH (Interventional)
'Observational' research includes: • Most projects involving data collection from a small number of patients. • Almost all projects conducted with previously collected *publicly available* data. • Non-interventional studies. Example: case-control studies, cohort studies, cross-sectional studies, case reports, case series, descriptive studies. • Projects involving simple non-invasive clinical examinations or educational tests. Example: Blood pressure testing, educational tests (cognitive, diagnostic, aptitude etc). • Research procedures using the following techniques: – Anonymous questionnaires (where identities cannot be traced in any way) – Coded (potentially identifiable) questionnaires or surveys – Identifiable surveys or questionnaires – Interviews (structured or unstructured), whether in person or by telephone – Web-based surveys The following studies will require in-depth review: • Major surveys or epidemiological studies involving extensive data collection from patients. • Research involving sensitive, personal or psychologically intrusive interview questions or questionnaires. • Studies involving the extraction of personally-identifiable information from health records. • Research using administrative or secure	'Clinical' research (unsponsored or sponsored) includes: • Interventional studies involving use of: drugs, therapeutic devices, surgical techniques or devices, diagnostic procedures or devices, dietary interventions, new indications for approved products. These also include randomization, withdrawal of treatment/services, or use of placebo. • Genetic research, human stem cells research • Interventional research involving vulnerable subjects (minorities, children, elderly, pregnant women, human foetuses, illiterate persons, prisoners or mentally-challenged subjects). • Interventional research that involves offering participants incentives to take part (which exceed reimbursement of travel costs, payment to compensate for work, etc).

data. *Example*: HID confidential databases • Research involving invasive procedures, *Example*: collection of body samples, medical procedures. • Research involving vulnerable subjects (minorities, children, elderly, pregnant women, human foetuses, illiterate persons, prisoners or mentally-challenged subjects). • Research that involves offering participants incentives to take part (which exceed reimbursement of travel costs, payment to compensate for work, etc).	

Applications for approval of all observational research studies will be reviewed by the RTST, PHCRC, or SHCRC. For clinical research studies, applications will be reviewed by the HRC after National Health Regulatory Authority , authorization letter.

3. SCOPE FOR REVIEW

The following types of submissions are in scope for review:

a. Submission of Research Application for initial review
b. Resubmission of Research Application with corrections
c. Post-approval submissions (Protocol amendments, progress reports, study completion report, adverse event reports, and renewal of approval)

4. SUBMISSION

Submissions to the MOH Research Committees are reviewed on a first-come, first-served basis. Research committee meetings for review of new research are usually scheduled once a week (or less, depending on the number of submissions).

The Review Meeting dates and submission deadlines for each month will be posted separately on the MOH intranet and internet websites. These dates will be updates regularly. The first 5 submissions received by the deadline will be included on the Research Committee's agenda, if complete and ready for research committee review. The remaining submissions will be placed on the next agenda.

4.1. DOCUMENTATION REQUIRED

The following documents are **required** to be included in the submission package. The Documentation Checklist in Appendix B serves as a quick guide to ensure that there are no missing documents.

4.1.1. 'Observational' (non-interventional) research

a. A signed covering letter from the principal investigator to the chairperson of the relevant research committee (with the signature of the Department Head/Chairperson/head of the research body).

b. Completed, signed and dated Research Application Form.

c. Curriculum vitae of the Principal Investigator *(applicant)*and co-investigator(s)

d. Detailed Research proposal

e. Participant recruitment material: advertisements, information letters

f. Informed consent form on the principal investigator's/Institution's letterhead (Arabic and English).

g. Data collection tools (e.g. questionnaires, data collection forms, etc.)

h. Number of centres and sample size for each centre (for multi-centre studies)

i. Project timeline

For student research, please also include:

j. *Supporting letter from* the Research Supervisor/Administration-in-charge/Head of the research body (on official letterhead).

k. Approval letter from the Ethics Review Board of the institution (on official letterhead).

4.1.2. 'Clinical' (interventional) research

a. Authorization letter from National Health Regulatory Authority

b. A covering letter from the principal investigator to the chairperson of the Health Research Committee (with the researcher's Department Head/Chairperson's signature/Head of Research).

c. Completed, signed and dated Research Application Form.

d. Curriculum vitae of the Principal Investigator (applicant)and co-investigator(s)

e. Detailed Protocol, including amendments to the protocol, if any

f. Investigator's brochure/Product monograph (for clinical studies involving a pharmaceutical/ biological/device product)

g. Participant recruitment material: advertisement, information letters

h. Informed consent/Informed assent form in English

i. Informed consent/assent form in Arabic (with signature and seal by a certified translator/translation service)

j. Data collection tools: Case Report Form, questionnaire, etc.

k. Patient instruction card, identity card, diary, etc.

l. Regulatory permissions (approvals from other Ethics Review Boards, FDA, EMA, etc.)

m. Signed agreements/contracts between different parties:
   - Investigator / institution and sponsor
   - Investigator / institution and CRO
   - Sponsor and CRO

n. No. of centres & sample size for each centre (for multi-centre studies)

4.2. DIRECTING YOUR RESEARCH APPLICATION

Research applicants must direct their applications to the relevant MOH Research Committees according to the guidelines below:

Observational Research

a. MOH Primary Healthcare staff and Family Practice Residency Program (FPRP) residents who intend to conduct research within a primary health care centre must submit their applications to the PHCRC.

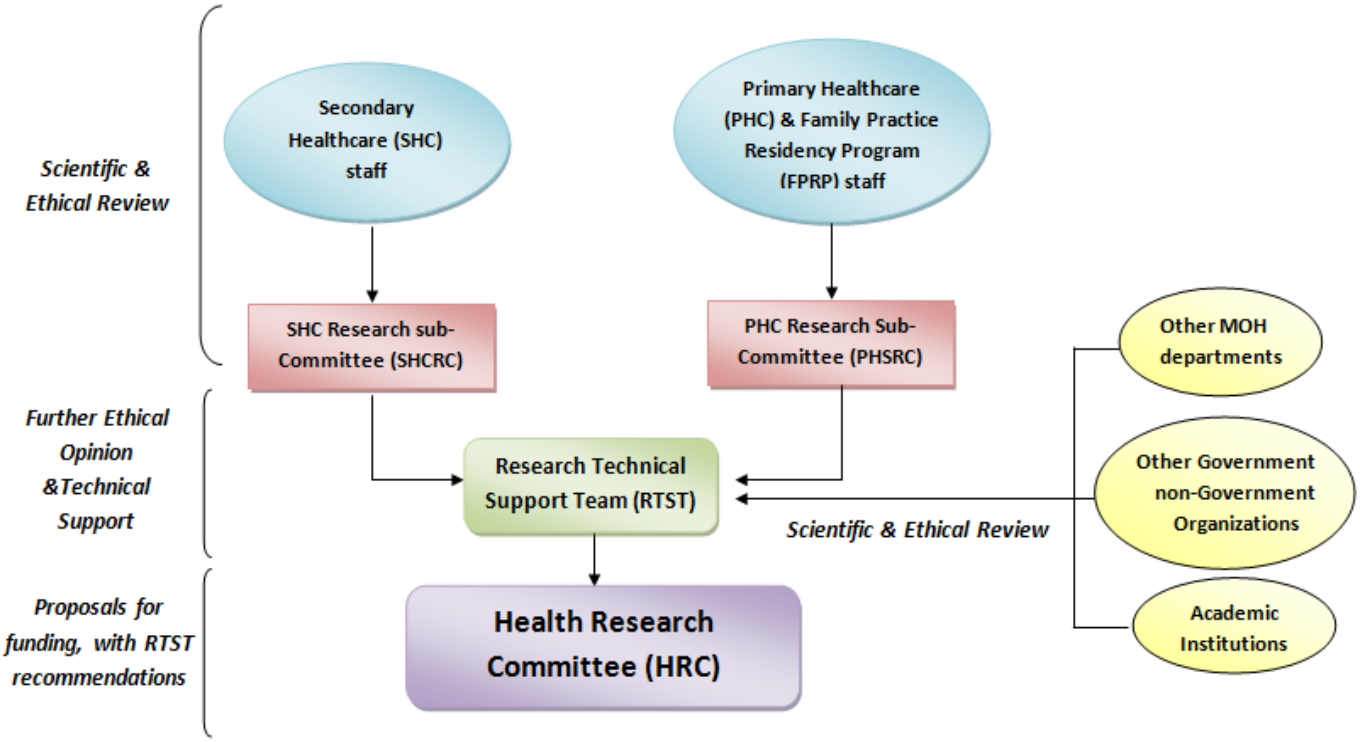
b. Staff from MOH secondary healthcare facilities and Salmaniya Medical Complex (SMC) staff who intend to conduct research within SMC or any of the secondary healthcare centres must submit their applications to the SHCRC.

c. Applications from other MOH staff, faculty/students of academic institutions, government and non-government staff, and from external sponsors (e.g., pharmaceuticals) must be submitted to the RTST.

d. Applications for national surveys from any applicant must be submitted to the RTST.

Following review, the PHCRC and SHCRC may forward applications requiring further scientific / ethical opinion and/or research funding to the RTST. Projects that need funding are assessed by the RTST for priority and validity, and subsequently recommendations will be raised to the HRC.

Figure 2 Flowchart (Observational Research): Where should you direct your Research Application?



Clinical Research

Any applicant (MOH staff or external researchers) who intends to conduct clinical trials within an MOH health care facility must first direct their application to the National Health Regulatory Authority (NHRA). The NHRA is the legal and national regulatory body responsible for approval of clinical trials. Following NHRA autherization, the applicant must prepare an application to the HRC for MOH authorization. The ethical, legal, and financial aspects of the clinical trial will be reviewed extensively by the HRC prior to granting approval.

If you have questions on where to direct your research, please send in your queries to the RTST Research Coordinator, Manal Hassan at RTST@health.gov.bh / or call on +973-17286052.

4.3. CONTACT DETAILS FOR SUBMISSION

One electronic copy of research applications (including all supporting documents as mentioned in Section 4) can be sent, email / fax to the relevant MOH Research Committee. The contact details for each of the MOH research committees are listed below.

Primary Healthcare Research Committee:

Chairperson: Dr. Ebtisam Mohamed Fakhro
Consultant Tutor, Directorate of Health Centres

POSTAL ADDRESS	PHYSICAL ADDRESS
Amira Ali Hammad, Medical Secretary - FPRP, The Office of FPRP, P.O.Box-42, Ministry of Health, Manama, Kingdom of Bahrain.	Amira Ali Hammad, Medical Secretary - FPRP, The Office of FPRP, Al-Naim Health Centre, Building 95, Lulu Road, Block 303, Kingdom of Bahrain.

Contact hours: 8:00 a.m. to 1:00 p.m., Sunday to Thursday.

Telephone: +973-17263597; Fax: +973-17251104

E-mail: AHammad1@health.gov.bh

Secondary Healthcare Research Committee:

Chairperson: Dr Eman Fareed

Consultant, Laboratory Department,
Salmaniya Medical Complex

POSTAL ADDRESS	PHYSICAL ADDRESS
Sawsan Ebrahim, Research Secretary, Ophthalmology Department, Salmaniya Medical Complex, P.O.Box-12, Manama, Kingdom of Bahrain.	Sawsan Ebrahim, Secretary, Administration Ophthalmology Department, Salmaniya Medical Complex, Kingdom of Bahrain.

Contact hours: 8:00 a.m. to 1:00 p.m., Sunday to Thursday.

Telephone: +973-17285041; Mobile: +973-39007273

E-mail: SEbrahim1@health.gov.bh

Research Technical Support Team:

Chairperson: Dr. Mohammed Amin Al-Awadhi
Assistant Undersecretary for Training and Planning
Directorate of Training and Planning, Ministry of Health

Deputy Chair: Dr. Najat Abulfath Ali
Chief, Medical Review Office

POSTAL ADDRESS	PHYSICAL ADDRESS
Manal Hassan Research Coordinator, Medical Review Office, Ministry of Health, P.O.Box-12, Kingdom of Bahrain.	Manal Hassan Research Coordinator, Medical Review Office, Flat 121 Ministry of Health, Building 1228, Road 4025, Block 340, Juffair, Kingdom of Bahrain.

Contact hours: 8:00 a.m. to 1:00 p.m., Sunday to Thursday.

Telephone: +973-17286052; Fax: +973-17286651

E-mail: RTST@health.gov.bh / Manal Hassan

4.4. SUBMISSION PROCESS

Received submissions are subjected to a preliminary screening and are checked for completeness by the Research Coordinator. An email acknowledging receipt submission will be sent to the researcher as documentation, containing a list of documents received, date of submission and comments on missing documents /preliminary queries.

5. REVIEW TIMEFRAME & PROCEDURE

The approximate target time between submission of a research application and final approval is estimated to be about 2 weeks (14 working days) for observational research, stretching to a maximum of 3 months (90 working days) in cases of clinical research projects.

a. Following the receipt of a **complete submission package**, the Research Coordinator creates an application reference number, assigns a review meeting date and distributes the package to the MOH Research Committee members for review.

b. Based on the risk-level of the research study, submissions are assigned for either a *full* or *expedited* review.
   - Protocols under **expedited review** undergo faster approvals (2 weeks for approval).
   - Protocols under a **full review** require longer review periods (4 weeks for approval).

c. The MOH Research Committee may invite an applicant to a review meeting to present his/her project and to clarify points where there is lack of clarity.

d. For cases requiring further consultation, a subject expert may be requested to act as referee and provide scientific/ethical opinion.

e. Shortly after the protocol has been reviewed, any required revisions or requests for clarifications will be forwarded in writing to the applicant. Most protocols undergo at least 1 round of revision prior to approval being granted.

6. APPROVAL

The MOH Research Committee review may have one of the following outcomes:

a. ***Full approval:*** No concerns with the protocol or supporting documents. The researcher may proceed with the research.

b. ***Conditional approval*** (Minor revisions required): Overall, the research project is satisfactory with minor modifications to be made. The researcher may proceed with the research only after making the requested changes. In this case, the researcher must submit an acknowledgement letter confirming that the committee's comments have been taken into account.

c. ***Re-submission*** (Major revisions required): Major methodological or ethical questions exist. Recommended revisions must be incorporated and the application re-submitted to the MOH Research Committee for a second round of review.

d. ***Rejection***: The committee may reject the application if:

   - The project is found to be too ethically controversial;
   - If the research methodology is scientifically flawed;
   - If the potential harm to the patients outweighs the benefits; or
   - If the researchers are not adequately qualified.

   The research committee shall provide the researcher with a letter stating the reasons for rejection.

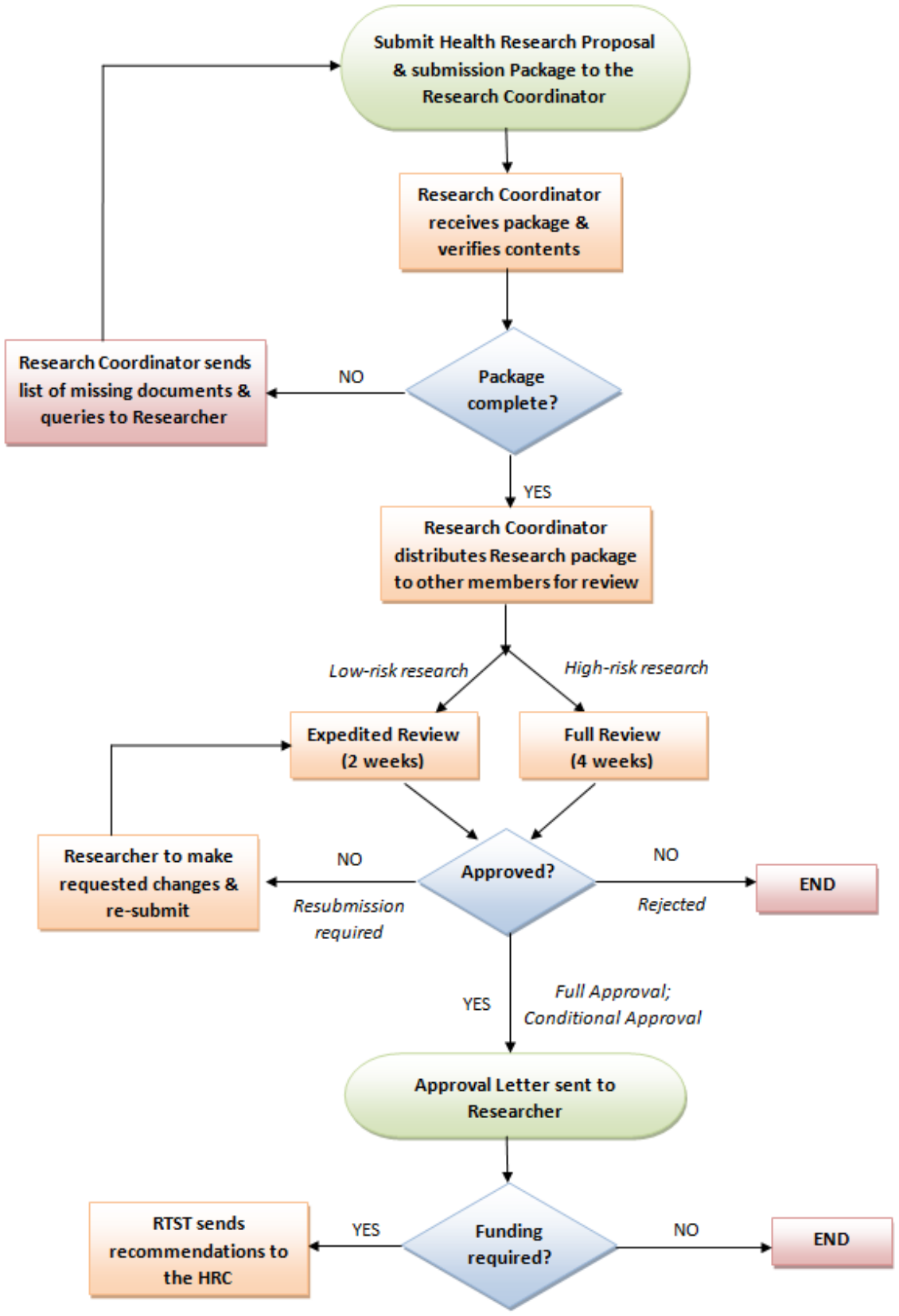
6.1. APPROVAL LETTERS

Following approval of the research project, researchers will be notified of approval by email, followed by a signed approval letter specifying the terms and conditions that apply to the approval.

Once obtained, researchers should retain their approval letters, as these specify the effective date of approval and the terms and conditions of the approval. Approved research projects must begin within 6 months of the date of approval.

For greater-than-minimal-risk research projects, approvals are issued for a period of 12 months only. For projects ongoing for longer than one year, researchers must submit an Annual Renewal Report (Section 9.3) prior to the expiry of approval in order to have their approval extended.

Figure 3 Flowchart - Research Review & Approval Process



7. APPEALING A RESEARCH COMMITTEE DECISION

When the MOH Research Committee (1) requires additional conditions before approving a protocol (conditional approval), (2) rejects a research proposal, or (3) judges a protocol deviation or violation to be sufficiently serious to merit calling a halt to ongoing research, **appeals** may arise because the Principal Investigator (PI) objects to the decision of the research committee and wishes to request a reconsideration to the decision made.

Researchers are entitled to request, and the MOH Health Research Committee has an obligation to provide, a reconsideration of a negative decision made by the relevant research committee that reviewed their proposal.

The researcher has 14 days from the date of written notification of the MOH research committee's decision to make an appeal. Appeals may ***only*** be heard on the basis of a procedural error that may have adversely influenced the decision of the MOH Research Committee, including real or reasonably perceived bias, epistemological bias (bias caused due to knowledge that the reviewer *believes* to be true), or undeclared conflict-of-interest on the part of one or more members of the Research Committee.

Appeals will be considered ***only in writing***, of decisions made by the peripheral sub-committees or made by the RTST itself. MOH Research Committee members, who were members of the original reviewing sub-committee, shall not take part in the appeal discussion, review or decision. At the discretion of the appeal panel, the investigator may be invited to the meeting at which his or her appeal will be considered.

7.1. HOW TO SUBMIT AN APPEAL

a. Please contact the RTST Research Coordinator, , either by email: or by phone: +973-17286052 to enquire about the date of the next RTST review meeting and to ensure that you submit your appeal on time (30 days in advance of the meeting date).

b. Applicants (appellants) must provide a Letter of Appeal to the Chair of the RTST which includes the following:

   - The Application reference number that was assigned to your original submission for review.
   - Your request to the RTST to appeal the decision made by the RTST itself or the relevant sub-committee.

- Details of the decision you received from the original reviewing committee and how you addressed the points raised.
- Justification for raising the appeal.
- Signed paper copy of your Application Form including any amendments/revisions already made, and all supporting documents.
- A letter from the Research supervisor/Head of medical staff supporting your appeal (desirable but optional).

c. Please submit the Letter of Appeal and the full set of appeal documents to the Research Coordinator **by email**.

7.2. NOTIFICATION OF THE APPEAL PANEL'S DECISION

During the appeal hearing, the panel may invite the appellant to meet with them to clarify points where there is a disagreement, or a lack of clarity. If additional expertise is required, the Chair may invite up to two members of staff with relevant expertise but who have not been involved in the initial decision to join the appeal hearing. After the hearing, the appeal panel will determine whether the applicant is successful.

A letter from the Chair of the RTST will be sent to the appellant within a week after the hearing, notifying them as to whether the decision of the original reviewing committee has been upheld or not. **The appeal panel's decision is final.**

8. RESEARCH FUNDING

8.1. ELIGIBILITY

The HRC will fund research projects that require financial support, provided that the general instructions (Section 1) and the following eligibility criteria are met. Funding is restricted to full-time MOH staff and will be in the form of *in-kind* contributions such as technical support and bearing of indirect costs. The researcher should:

a. Ensure that the research is related to, and will focus on the identified health research priorities for Bahrain and the 6 strategic goals of the Bahrain Healthcare Agenda – Health Improvement Strategy, 2015-2018.

b. Ensure the potential of introduction of the research findings into policy and practice in the Bahrain healthcare system, and

c. Ensure scientific soundness of the project.

8.2. EXCLUSION CRITERIA DURING PRELIMINARY SCREENING OF APPLICANTS FOR RESEARCH GRANTS

The following applicants may not be eligible for a research funding request:

a. Principal investigators with an ongoing research project funded by the MOH (Such applicants are eligible to apply for grants after the submission of their previous research reports).

b. Applicants who have sought funding from other agencies.

For research requiring funding, copies of approval letters are forwarded to the HRC, at which point the applications are reviewed for the awarding of research grants.

9. POST-APPROVAL REPORTING REQUIREMENTS

The following sections detail instructions for notification of amendments, adverse events or study completion following MOH Research Committee approval.

9.1. AMENDMENTS (Form 3)

Any changes made to either the research protocol (including changes to the study design recruitment method, study population, surveys, questionnaires, or interview formats), or the consent form must be submitted for review.

Researchers seeking an amendment should:

1. Complete the Amendment Request Form (Form 3), indicating request for approval of changes to an approved protocol.
2. Attach copies of any revised study documentation e.g., modified recruitment documents or altered protocol, as described in the form.
3. Submit the above to the concerned research committee for review.

Amendments can be minor (in which case the Chairperson of the Research committee can authorize their approval) or more substantial (in which case they are sent to one/more of the original reviewers of the protocol for assessment and approval). If the proposed amendment requires revision, or further information is needed, the researcher will be notified in writing. Once the amendment is approved, the researcher is provided with an amendment approval letter. Only after the amendment has been approved can the changes be implemented.

9.2. UNANTICIPATED/SERIOUS EVENT REPORTS *(Greater-than-minimal-risk research only)* (Form 4)

An **unanticipated adverse event** is defined as any adverse event or outcome experienced by any participant, which exceeds the risk that the participants were informed of during the consent process.

A **serious adverse event (SAE)** is an adverse event that:

- Results in death; or
- Is life-threatening; or
- Requires in-patient hospitalisation or prolongation of existing hospitalisation; or
- Results in persistent or significant disability or incapacity; or
- Causes congenital malformation/birth defect.

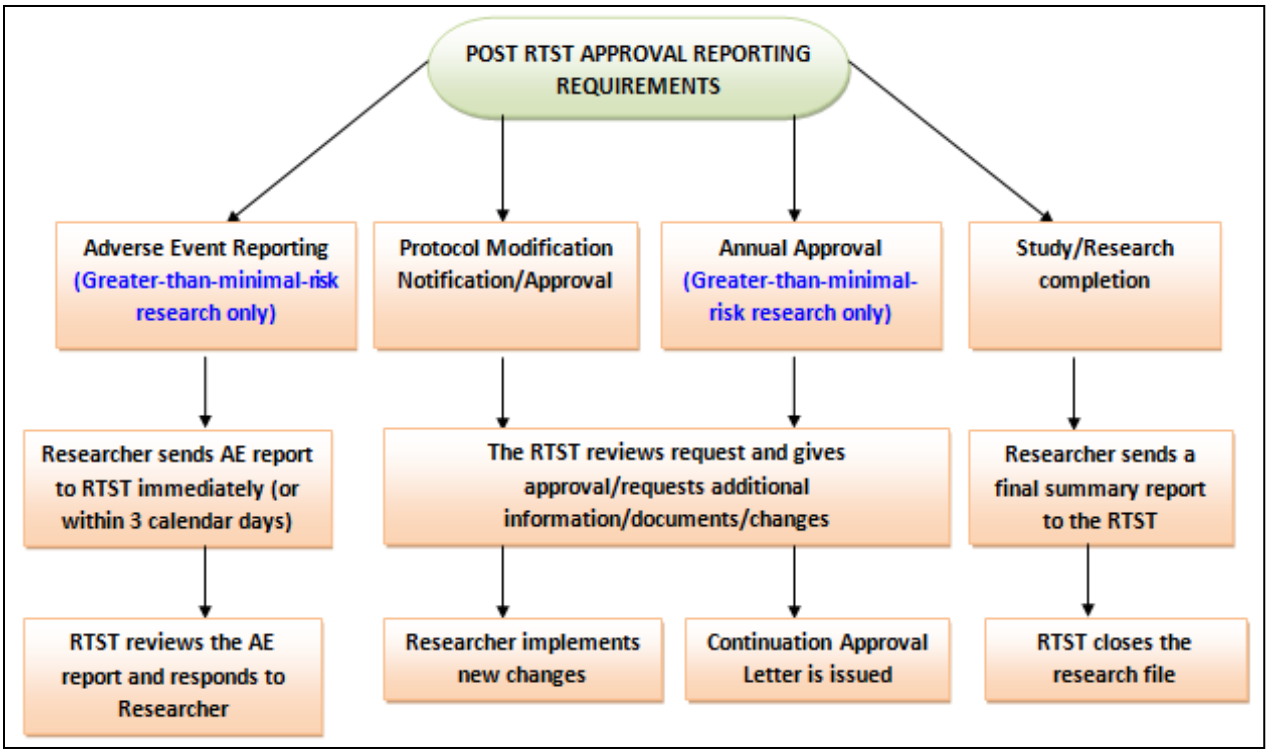
Should any unanticipated/serious adverse events occur in relation to a research project involving human participants, these **must immediately (maximum within three calendar days) be reported to the Chairperson of the concerned research committee** by a telephone call (Section 0) followed by a filled Unanticipated/ Serious Adverse event Report Form (Form 4).

9.3. ANNUAL RENEWAL REPORTS AND STUDY COMPLETION REPORTS (Form 5, Form 6)

For all projects, researchers are required to notify the research committee upon completion of the research study, and fill out a Study Completion Report (Form 6). Study completion is defined as the time point when it is clear that there will be no more requirements for data collection or analysis. Following submission of Form 4, the research committee archives the research file.

For greater-than-minimal-risk research projects extending beyond one year, researchers must submit an annual progress report for review in order to have their approval extended. Several weeks in advance of the expiry of their 12-month approval, researchers must submit a completed Annual Renewal Report (Form 5), **prior to the expiry date.** Should a research project be completed prior to the 12-month renewal date, the researcher must notify the research committee and complete the Study Completion Report (Form 6).

Figure 4 Flowchart: Post-Approval Reporting Requirements



10. ADDITIONAL CONSIDERATIONS

Researchers must be aware of the following additional considerations while conducting their research projects within MOH healthcare centres or while making use of MOH resources.

10.1. PARTICIPANT ANONYMITY AND DATA CONFIDENTIALITY

All health research using identifiable personal information or anonymised data from the MOH that is not already in the public domain **must be approved** by an MOH Research Committee.

Researchers should treat all personal and medical information as confidential. This applies as much to the results of laboratory tests done as part of the research project, as to information obtained directly from participants or their medical records.

All personal information must be coded or anonymised as far as possible and as early as possible in the data processing. Principal investigators have personal responsibility to ensure that procedures and security arrangements are sufficient to prevent breaches of confidentiality. **A breach of confidentiality is an illegal offence and is subject to legal action according to criminal law.**

10.2. COLLECTION OF BIOLOGICAL SAMPLES

All research using human biological samples **must be approved by an MOH research committee**, whether these projects involve use of newly collected samples or secondary use of samples collected for previous research.

10.2.1. Informed consent for collection of new samples

Informed consent **must** be taken from participants whenever a new sample is taken for the purposes of research. Research participants must understand what the sample is to be used for and how the results of the research might impact them. Consent must also be obtained for the storage and potential future use of samples. However, it is acceptable for researchers to use human material from a tissue/blood bank without participant consent if the samples are anonymous and unlinked.

When obtaining consent to take a biological sample for research, it is important to allow for the fact that it might subsequently be useful for new experiments that cannot be foreseen. Therefore, unless a sample will be used up fully for the initial project or cannot be stored, a two-part consent process is recommended, the participant being first asked to consent to the specific experiment(s) already planned, and then to give consent for storage and future use for related research.

10.2.2. Informed consent for secondary use of old samples

Secondary use of biological samples, whether previously collected for clinical purposes or for purposes of other research projects, may be authorised provided:

1. The new research proposal is approved by the MOH Research Committee.
2. The research subjects did not object to the use of their sample in future research projects.

The MOH Research Committee will decide on a case-by-case basis whether:

1. The new research is covered by the previous consent, if any, or
2. Subjects should be contacted to obtain a new consent, or
3. A consent can be waived

10.2.3. Disclosing results of laboratory tests to research participants

Research participants have a right to know individual research results that affect their interests. Researchers must decide at the beginning of a project what information about the results of laboratory tests done on samples should be made available to the participants or their clinicians, and share these plans with the MOH Research Committee. If research results have immediate clinical relevance, there is a clear duty of care to ensure the participant or his/her clinician is informed.

10.3. ACCESS TO PATIENT MEDICAL RECORDS AND IDENTIFIABLE INFORMATION FROM THE MOH

No more information than that needed to accomplish the study must be recorded. The datasheet which contains the information to be recorded must be submitted with the protocol for MOH Research Committee approval.

Following MOH Research Committee approval, access to paper or electronic medical records **require authorization from the official data custodian of the records** (e.g. Health Information Directorate, head of the medical record department of the appropriate health centre or hospital, or the patients' clinician).

10.4. PARTICIPANT COMPENSATION

The HRC believes that no amount of compensation or payment must be provided which will serve to coerce an informed subject to consent to participate. The principal investigator may be allowed to reimburse participants for:

a) Out-of-pocket expenses borne by the subject for travel, meals, etc
b) Degree of anticipated discomfort or inconvenience
c) Duration of the study and impact on work-related income and time lost from work.

The MOH Research Committee will review the compensation offered and ascertain the reasonableness of the compensation detailed by the researcher in the application. Additionally, the investigator must indicate the amount of compensation in the informed consent form.

11. FREQUENTLY ASKED QUESTIONS

A list of common queries will be posted on the MOH website with our responses. Researchers may refer to this to eliminate any doubts they may have on the Research submission and review process. For any further questions, you may contact the RTST Research Coordinator at +973-17286052

suggested reading

- Bahrain's Healthcare Agenda – Health Improvement Strategy 2011-2016; Ministry of Health, Kingdom of Bahrain, 2011.

- MOH Ethical Guidelines for Health Research, 2008. http://www.moh.gov.bh/PDF/Health%20Research%20Structure%20and%20Procedures%20%20DRAFT.pdf

- ICH Harmonized Tripartite Guideline for Good Clinical Practice ICH Topic E6), *Good Clin Pract J* 3:S3–S27.

- Protection of Human Subjects, Code of Federal Regulations, 21CFR50, Food and Drug Administration, USA.

- World Medical Association, Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects: Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and most recent amendments accepted at the 59th WMA General Assembly, Seoul, October 2008. http://www.wma.net/e/policy/b3.htm

- Council for International Organizations of Medical Sciences (CIOMS). International ethical guidelines for biomedical research involving human subjects. (Accessed November 10, 2011 at http://www.cioms.ch/publications/layout_guide2002.pdf)

APPENDICES