Shaukat Khanum
Memorial Cancer Hospital
and Research Centre

RESEARCH GUIDELINES

POL/C/CEN/CRO-001/v.6

Prepared by	Reviewed by	Approved by
Clinical Research Administrator	Director QPSD	Chief Medical Officer (CMO)
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Hospital leadership represented by Chief Executive Officer (CEO), Chief Medical Officer (CMO) and Medical Director (MD) is committed to do high quality research as reflected in the mission statement of the hospital, "To act as a model institution to alleviate the suffering of patients with cancer through the application of modern methods of curative and palliative therapy irrespective of their ability to pay, the education of health care professionals and the public and to perform research into the causes and treatment of cancer"

Leadership at SKMCH&RC promotes research of the highest scientific and ethical standards. It has established research guidelines to provide guidance to investigators. Research guidelines define the scientific standards and code of ethical conduct of research involving human subjects, which should be followed by all researchers of the hospital. These are based on ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good clinical practice (GCP) guidelines and the applicable regulatory requirements. Leadership has established this code to ensure the ethical conduct of research.

Hospital leadership accepts the accountability of protection of human subjects in all research activities of the hospital irrespective of the sponsor of the research. All research participants are entitled to treatment at SKMCH&RC. Leadership makes the investigators responsible for the protection of human subjects from research risk. Review Bodies (Scientific review committee, SRC and Institutional review board, IRB) are authorized to review this aspect. Clinical research office develops, maintains and disseminates these guidelines and ensures the compliance of researchers with these guidelines. Hospital leadership also provides resources and recognition for the performance of good research. The evaluation of staff participating in the research program is incorporated into the routine appraisal of professional performance. The hospital research program is integrated into the quality and patient safety program of the hospital to ensure safe, high-quality care for patients participating in research activities.

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1.0 STARTING A RESEARCH PROJECT AT SKMCH&RC

1.1 What is Clinical Research?

For the purposes of these guidelines, clinical research is defined as a systematic activity that involves one or more of the following:

- People (typically patients, their carers, staff or volunteers)
- Their tissue
- Their organs
- Their personal information

And that meets all three of these criteria

- Attempts to answer a clearly defined question
- Employs systematic and rigorous methods
- Leads to new knowledge that may be transferable/generalizable

The first two criteria will also be met by audit and service evaluation activities, but these differ from research in that audit seeks to measure existing practice against evidence-based standards, and service evaluation addresses local service issues.

You need to register your project if it involves participants for whom SKMCH&RC has a duty of care, i.e. patients, their carers or staff including data, images or tissue derived from the participants. You will also need to register your research if it occurs in SKMCH&RC premises even if it does not directly involve patients as would be the case of a medical physicist working on the development of instrumentation. You may begin your project only after you have received a formal letter of approval, following research review applicable to your research project

Some examples:

- If participants are recruited by virtue of their relationship with SKMCH&RC, but the study involves interviewing subjects in their own homes, the hospital has a duty of care.
- If the participants are recruited by virtue of their membership of a community group, and are interviewed on SKMCH&RC premises, SKMCH&RC has a duty of care.
- If the participants are recruited by virtue of their membership of a community group, and are interviewed in their homes, SKMCH&RC does not have a duty of care. In this case, if the subjects were recruited or identified because of lists/data available at SKMCH&RC, the research still falls under the purview of SKMCH&RC

1.2 Types of Research Projects Undertaken at SKMCH&RC:

All clinical departments at the hospital are involved in investigator-initiated studies and clinical trials. Following three sections housed in Abdul Hafiz Research Wing are dedicated to perform and facilitate research in variety of ways:

- Clinical Research Office
- Basis Science Research Lab
- Cancer Registry and Clinical Data Management

Pharmacy, nursing, radiology, pathology, ancillary teams and other relevant services also provide support for various research studies where required. Human subject research activities in diverse areas related primarily to the diagnosis and treatment of cancer are undertaken at the hospital. We are currently not involved in animal research activities.

Table 1 below gives an overview of the various types of research projects undertaken at the hospital and their approval requirements.

Type of Work		**Purpose**	**Scientific Review**	**Ethical Review**
Informal review	Typically < 50 charts	Exploring ideas	No	Only if report generated
Clinical Audits	Quality assurance (QA) activity	QA audit and service evaluation	No	No
Non-interventional Research	Descriptive studies such as case report (n=1) and case series (n≤3) and retrospective studies involving existing data	Non-Analytic Research	No	Yes (exemption granted if based on anonymized existing data)
	Analytic studies such as case-control, cohort and cross sectional studies (includes studies involving human biological material and images)	Analytic Research	Yes	Yes

Interventional Research	Clinical trials (Randomized and non-Randomized including research with behavioral and social interventions)	Experimental Research	Yes*	Yes
	Other experimental studies such as qualitative research studies , quasi-experimental studies etc.	Experimental Research	Yes	Yes

Table 1: Types of Research Projects Undertaken at SKMCH&RC

* Scientific review in case of international multicenter investigational new drug /device/biologics trials is done during the internal feasibility assessment process facilitated by the Clinical Research Office. Proposed investigators, who are subject area experts, are part of this assessment and studies are reviewed for both scientific content and their logistic feasibility at the hospital.

Research studies to be done in collaboration with other organizations would require additional steps which may involve IRB review at collaborating institute, collaboration data/material transfer and funding agreements, and other applicable regulatory requirements as per national and international laws and regulations. No collaborative research can be undertaken without the involvement of a designated member of SKMCH&RC staff as the institutional facilitator for that project. (See section 6 for details.)

1.3 Conducting Research at SKMCH&RC

- **Registration of research -** Registration of research is done by submission of the research studies to the clinical research office. Complete guidance on how to make a submission of research study is provided in the Appendix I Clinical research office shall facilitate scientific and ethical review of studies as applicable.

- **Scientific review -** The MD will nominate a scientific review committee for projects that qualify for scientific review. SRC is constituted wilth MD, Secretary SRC, Secretary IRB, at least two members from the consultant staff and at least one representative from the basic science research group and the cancer registry and clinical data management (CRCDM) section . The committee will advise and facilitate the investigators and may support, oppose or suggest modifications to the proposal.

- **IRB approval** - Once scientific approval is obtained, the study should be submitted for approval by the IRB. Clinical research office staff will guide and facilitate the principal investigator in

this process. The primary objective of obtaining IRB approval is to ensure the protection of the rights, safety and well-being of study participants and to address ethical issues. The IRB may approve, reject, modify or defer pending further information. Research projects which fall in the following categories also need to be submitted to the Research Ethics Committee (REC) of the National Bioethics Committee (NBC), Pakistan for review and approval before these are initiated

- All research (medical or social science) projects involving human subjects, whether as individuals or communities, including surveys, drug/device trial, the use of fetal material, embryos and tissues from alive or the recently dead done with one or more of the following
    - International funding specifically given for research done anywhere in Pakistan e.g. Research Advocacy Fund (RAF), DFID, USAID etc
    - Funded or supported by the Government of Pakistan
    - Any other research either done all over Pakistan or is a multi-province
    - Drug trials for registration

  Click here to download NBC application form, exemption request form and guidance sheet (used with thanks and permission of National Bioethics Committee, Pakistan)
  http://nbcpakistan.org.pk/downloads.html

- Human subject research involving no more than minimal risk qualifies for exemption from full quorum IRB review. These studies will not require approval by SRC as the scientific and ethical review is completed jointly by designated IRB members. Appendix I contains detailed guidance on which type of projects may qualify for IRB exemptions.

- **Application for SKM funds (if applicable)**

- **Maintenance of a site file and research records -** This includes essential documentation related to the study such as protocol, signed consent forms, case report forms/source data , ethics review approval and related communication record, regulatory approval (where applicable), medication management records (in case of studies involving investigational new drug/device/biologic interventions), hazardous material management and maintenance of equipment used in research (if applicable). Investigators should retain a record of study team qualification and delegation of study related duties as per their qualification and experience. In addition , a record of research oversight by the principal investigator or training supervisor as applicable should be maintained . For interventional drug/device /biologic studies, reporting of adverse events as per hospital adverse event reporting (ADR) system should be ensured along with the sponsor and IRB reporting requirements. In addition, all incidents , sentinel events and near misses in a research participant should be reported as per the hospital quality improvement (QI) and sentinel event reporting system. Clinical research shall educate researchers on responsible conduct of research and research-related documentation requirements for all prospective research studies via series of research oversight meetings (for details see section on investigator's responsibilities on resposible conduct of research)

- **Preparation of periodic progress reports -** IRB at SKMCH&RC collects periodic progress reports for all IRB approved studies reviewed by the full quorum committee as per frequency defined by the IRB (at least annual frequency). In addition, investigators are required to submit all amendments to the protocol for IRB review and approval as well as a final report at study completion. Investigators are also required to notify the IRB in case of changes in the study team.

- Research Compliance and Integrity Oversight: As part of hospital's commitment to facilitate researchers in ensuring responsible research conduct, a representative from the clinical research office team meets investigators of all prospective studies, periodically, during the course of the study to provide guidance on appropriate record keeping for research and to enhance awareness of researchers about responsible research conduct. At study close out, all study records are collected at clinical research office for central archiving and retained as per hospital record retention and archival policy.

1.4 Submission Requirements

For details related to submission Requirements, kindly see appendix I.

The following general format should be used as guidance for submitting a synopsis and related documents (such as Informed consent forms etc.) for review and approval;

I. **Study Title**
II. **Investigator(s) With Institutional Affiliations**
III. **Introduction**
IV. **Objectives**
V. **Definitions**
VI. **Hypothesis**
VII. **Materials And Methods**

Study Design: Describe in detail the design and methodology of the study. Identify and distinguish between those procedures that are standard of care and those that are experimental. Provide a detailed description of the planned data collection, specific outcomes, and criteria for evaluation and endpoint definition.

Setting

Duration: Include the frequency and duration of each activity and the total length of subject participation.

Sample Size and Sampling Techniques: If applicable; include information on stratification or randomization plans, the maximum number of subjects you plan to recruit for this study. If this is a multi-site study, indicate the projected total subject accrual.

Inclusion and Exclusion Criteria

Study Procedures: Include details on medical procedures

Data Analysis and Statistical Methods: Describe the statistical considerations for the study, how the sample size was determined, and how the results will be analyzed, if applicable.

For Interviews/Focus groups: Attach copies of any scripts and/or questions that will be used to guide the interviews/groups. Indicate the member(s) of the study team who will conduct the interviews/focus groups and any necessary qualifications such as special training, supervision etc.

For Studies Involving Surveys/Questionnaires: List all of the measures/instruments that will be used for this study and attach copies for these. Indicate the member(s) of the study team who will use these measures/instruments and any necessary qualifications such as special training or licenses.

For Studies Involving Use of Existing Data/Specimens: When using existing data/specimen and Applying for Exemption, Describe the following: the source of data/specimen and the process used to unlink the data or specimen/make it anonymized/ (the process by which identified data is recorded in a way that individuals cannot be identified)

VIII. HUMAN RESEARCH SUBJECT PROTECTION

Risks, Discomforts and Potential Harms: Describe the risks associated with each research intervention (physical, psychological, social, and other factors) with the estimated probability that given harm may occur and the potential reversibility. Describe the safety precautions that will be taken to minimize risks/harms. When appropriate, include a study monitoring plan for the safety of participants and for the validity and integrity of data.

Potential Benefits and Alternatives:

Describe any potential for direct benefits to participants in the study. There may be no direct benefits. Also, include information on the importance of the knowledge that may reasonably be expected to result. Also describe the alternatives available to patients in cases of non-participation in research.

Informed Consent: Indicate the types of consent that will be involved in this study and attach copies of the informed consent/assent document that will be used for this study. If a waiver of Informed consent is considered justified, describe with reasoning.

Data Privacy and Confidentiality: How will the data for this study be collected and recorded? Describe the provisions to protect the privacy of the individual. Where will the research data be stored & how it will be secured? Who will have access to the study records or data? Specify their name, role and affiliation.

IX. RESOURCE REQUIREMENT

Monetary, logistic and administrative or other

X. REFERENCES

2.0 ENSURING GOOD CLINICAL PRACTICE IN RESEARCH

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting research that involves the participation of human subjects. Compliance with this standard provides assurance that the rights, safety and well-being of research subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

2.1 Definitions

When considering applications that involve human subjects, it is important for reviewers and researchers to keep a number of definitions of terms in mind:

Human subjects: A "human subject" is defined as a "living individual about whom an investigator obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information."

The **regulations** extend to the use of human organs, tissue and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. A subset of research involving human subjects may qualify for the exemption, but justification must be provided

Children: For purposes of this policy, a child is an individual under the age of eighteen (18) years.

Clinical research is defined as:

(1) Patient-oriented research, i.e., research conducted with human subjects (or on the material of human origins such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. (Excluded from the definition

of patient- oriented research are in vitro studies that utilize human tissues that cannot be linked to a living individual).
Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) research projects, and (d) development of new technologies; (2) epidemiologic and behavioural studies; or (3) outcomes research and health services research.
A clinical trial is operationally defined as a prospective biomedical or behavioural study of human subjects that is designed to answer specific questions about biomedical or behavioural interventions.

Investigator: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Co-Investigator: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., research associates/ coordinators, residents, research fellows etc.).

Sponsor: An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial

Contract Research Organization: A person or an organization (commercial, academic, or other) contracted by the research sponsor to perform one or more of a sponsor's trial-related duties and functions

Randomization: The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Blinding/Masking: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), the investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

A **clinical trial** is a broadly based prospective clinical investigation, involving human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioural interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

A **valid analysis** is required for all research projects. This means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies.
A valid analysis does not need to have high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis are:

- Allocation of study participants of both sexes/genders and different racial/ethnic groups to the intervention and control groups by an unbiased process such as randomization (applicable for studies using a randomised controlled design)
- Unbiased evaluation of the outcome(s) of study participants, and
- Use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects among the sex/gender and racial/ethnic groups.

Adverse Event (AE): Any untoward medical occurrence in a research participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR): Any untoward medical occurrence that at any dose:
– results in death,
– is life-threatening,
– requires inpatient hospitalization or prolongation of existing hospitalization,
– results in persistent or significant disability/incapacity,
or
– is a congenital anomaly/birth defect.

2.2 Protection of Human Subjects

If the proposed research involves human subjects, reviewers must evaluate the plan to protect human subjects. The applicant's research plan should include details about the protection of human participant from research risk. Reviewers are asked to evaluate the following elements of human research participant protection:

Risks to the research participants: discussion of research participant involvement and characteristics, source of material, and potential risks. This includes a discussion of the likelihood and seriousness of the potential risk to subjects including, if applicable, risks to vulnerable populations and hospital staff (such as the potential for coercion and undue influence). Where appropriate, alternate treatments and procedures, including risks and benefits, should be considered. If a test article (Investigational New Drug, device, or biologic) is involved, or if the applicant proposes using a drug or device in a method that may not have regulatory approval, the test article must be named and the status with regard to regulatory approval by international (e.g., Food and Drug Regulation Authority, FDA) and local (Drug Regulatory Authority of Pakistan, DRAP) regulatory bodies must be stated.

Adequacy of protection against risks: discussion of plans to protect against or minimize potential risks and assessment of their likely effectiveness. Where appropriate, this should include discussion of plans for ensuring necessary medical or professional intervention in the case of adverse effects.

Also included are recruitment plans and description of the process for obtaining informed consent, including the information to be provided to subjects. It will be ensured that for any

collaborative/sponsored research study/trial, appropriate indemnity is in place. For institutional research projects, the hospital will provide management of adverse effects.

The potential benefit of the proposed research to the research participant and others: discussion of why the anticipated risks are reasonable in relation to the anticipated benefits to the subjects and to others.

Importance of the knowledge to be gained: discussion of why the risks to subjects are reasonable in relation to the importance of the knowledge to be gained.

There is a fifth level of protection involving data and safety monitoring if a clinical trial is proposed. All such applications should include plans for data and safety monitoring and should follow the institutional policies and procedures for adverse event reporting.
Based on the evaluation of whether the applicant has adequately addressed human subjects protection according to these criteria and subsequent discussion, the reviewer may score the application with no concerns or with comments or concerns that may affect the score to a level commensurate with the seriousness of the concern.

2.3 Biohazards

The investigator and the sponsoring institution are responsible for protecting the environment and research personnel from hazardous conditions. As with research involving human subjects, reviewers are expected to apply the collective standards of the professions in identifying potential hazards, such as inappropriate handling of oncogenic viruses, chemical carcinogens, infectious agents, radioactive or explosive materials, or recombinant DNA. If applications pose special hazards, these hazards will be identified and any concerns about the adequacy of safety procedures highlighted. The inventory, handling, storage, and use of hazardous materials and waste in research studies will be carried out as per hospital policies.

2.4 Confidentiality and Communications with Investigators

All materials pertinent to the applications being reviewed are privileged communications prepared for use only by consultants and other SKMCH&RC staff, and should not be shown to or discussed with other individuals. Review group members must not independently solicit opinions or reviews on particular applications or parts thereof from experts outside the pertinent initial review group. Members may, however, suggest scientists from whom the SRC may subsequently obtain advice. Consultants are required to leave all review materials with the SRC secretary at the conclusion of the review meeting. Privileged information in grant applications shall not be used to the benefit of the reviewer or shared with anyone.

Under no circumstances shall consultants advise investigators, their organizations, or anyone else of recommendations or discuss the review proceedings while the review process is ongoing. The investigator may be led to unwise actions on the basis of premature or erroneous information. Such advice also represents an unfair intrusion into the privileged nature of the proceedings and invades the privacy of fellow consultants serving on review committees. A breach of confidentiality could deter qualified consultants from serving on review committees and inhibit those who do serve from engaging in a free and full discussion of recommendations.

Ordinarily, there must be no direct communications between consultants and investigators. Consultants' requests for additional information and telephone inquiries or correspondence from investigators must be directed to the SRC, who will handle all such communications.

2.5 Scientific Misconduct

" Research Misconduct" or "Scientific Misconduct " is defined as fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting or reporting research. It does not include honest error or honest differences in interpretation or judgments of data.

The reviewers should not review an application about which an allegation of misconduct has been made . The SRC/IRB secretary should report the allegation to the MD. In all cases of suspected misconduct, it is essential that the SRC/IRB secretary stress to the reviewers the seriousness of such allegations and the potential harm that may result if confidentiality is not strictly maintained. In addition, it is important for the SRC/IRB to assure the reviewers that the suspicions identified will be taken seriously and pursued by the MD.

2.6 Conflict of Interest

Conduct of research at SKMCH&RC needs to be of high standards and calls for the declaration of conflict of interest, enabling further actions to either eliminate, reduce or manage such conflicts, as appropriate. It is in line with the hospital policy on conflict of interest.This policy applies to both researchers as well as reviewers of research and those making funding decisions.

2.6.1 Guidance for Reviewers:

A conflict of interest (COI) exists when a reviewer or chair of review committee has certain relationships to research protocols that the Institutional Review Board (IRB) or Scientific Review Committee (SRC) reviews.

This includes participating in or supervising the research project, a financial interest, a personal interest, or some other situation giving rise to a conflicting interest.Peer review system is subject to academic conflict of interest when one reviewer may critique or delay competitor's research proposal to strengthen his or her own chances of funding or promotion or may respond positively to one proposal which may lead to intangible personal gain.

The reviewer conflict of interest declaration should be signed by all reviewers as well as chair of review committee, after they have reviewed the agenda (list of research studies under review). Medical director would make the final determination. No reviewer will be allowed to participate in the review of research in which the member has a conflicting interest, except to provide the information requested by the SRC/IRB.

2.6.2 Guidance for Researchers:

All researchers must identify and declare any conflicting interests related to their research at the time of submitting it to for review. Conflicting interests exists when professional judgment/practice concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or professional rivalry). It may arise for researchers when they have a relationship with sponsoring company (paid or honorary position on advisory board or steering committee, sponsorship of symposium or meeting, or a travel grant), which may influence their interpretation of efficacy of the product of the sponsor or reporting of serious adverse events.

Researchers are required to disclose such relevant information while submitting their studies via a COI form available at the research office. Medical Director will make final determination and advice on the matter under review.

Clinical research office will educate all reviewers and researchers to complete and submit a signed conflict of interest forms in a timely manner and ensure compliance to above. Following are the examples of possible financial conflicts of interest;

- A fee for speaking
- A fee for organizing educational activity
- Reimbursement for attending a symposium/conference/meeting etc
- Sponsorship of your research or that of your trainees
- Paid or honorary position on advisory board or steering committee
- Employment
- Any sponsorship/funding that investigators may have received to help conduct a study.

2.6.3 Monitoring Process for Conflict of Interest Declaration :

The conflict of interest declaration will be evaluated by relevant heads of department before final review by the Medical Director who will evaluate such conflicts and if necessary, determine

1. Whether the conflict is permissible in the context of the proposed research
2. Whether the conflict warrants disclosure to potential participants as part of informed consent process or
3. Warrants further management to reduce or eliminate the interest.

The medical director will communicate when it is determined that interest must be disclosed and/or further managed. Monitoring reports of conflict of interest is presented to Clinical Exective Board (CEB).

2.7 Process for Scientific and Ethical Review of Research

Each research activity undertaken at the SKMCH&RC hospitals needs a prior review and approval by relevant research committees. Researchers are encouraged to review Appendix I for detailed guidance for research review requirements and process.

2.8 Scientific Review Committee

An independent hospital committee, which is responsible for reviewing the scientific content of research protocols. Research projects which are conducted at SKMCH & RC need approval from the SRC prior to IRB presentation.

2.8.1 Terms of Reference

1. The Scientific Review Committee (SRC) will be chaired by the Medical Director (MD), Lahore. A fulltime secretary to the SRC will assist the principal investigator (PI) in obtaining approval from the SRC.
2. All necessary documentation must be completed & submitted to the secretary SRC by the principal investigator at least four weeks prior to the scheduled date of the meeting.
3. SRC will have representation from all hospitals of Shaukat Khanum Trust and at least one representative each from the basic science research lab and cancer registry and clinical data management (CRCDM) as permanent members. Chair will also nominate two reviewers for each research study.
4. SRC will ensure that the proposed study is appropriate for the institution
    a) Target patient population, infrastructure and facilities are available
    b) Investigator and research team suitability for carrying out the research study

5. The SRC will meet once per month or frequently if needed.
6. The secretary SRC will make sure that final versions of the following documents are sent to reviewers at least two weeks prior to the meeting:

- Copy of clinical research protocol (and any amendments)
- A copy of investigator brochure and any available safety information
- Proposal review request

7. In the meeting, the Principal investigator will present the protocol under review and answer any questions posed by the reviewers. In the event of serious objections, re-submission of the protocol, with amendment will be necessary. Ordinarily, the purpose of the second meeting will only be to address issues raised following the first meeting.
8. The assigned scientific reviewers must ensure submission of their complete critique of the submitted proposal before the SRC meeting and presentation by the PI.
9. Decisions in the SRC will be based on consensus. The Medical Director will have final authority in case of a dispute.
10. If required, the medical director (MD) may obtain assistance and advice from outside reviewers.
11. No protocol will be presented to the IRB before the SRC issues its written approval, except in the following circumstances

- Studies qualifying for exempt status are submitted directly to IRB (see the section on IRB review for details)
- For international investigational new drug (IND) / device or biologics trials, the scientific review will be carried out during the initial feasibility assessment process coordinated through the clinical research office. The process involves assessment of scientific validity, availability of target population, infrastructure and facilities which is carried out by proposed investigators who are subject area experts, in liaison with clinical research office.

12. The secretary SRC will be responsible for maintaining all relevant records (e.g. written procedures, submitted documents, minutes of meetings & correspondence) for a period of at least three (3) years after the completion of the study and make them available if required by regulatory authorities.
13. To obtain the application template, guidelines for SRC approval and for any further information regarding SRC approval contact:

Clinical Research Administrator
Shaukat Khanum Memorial Cancer Hospital & Research Centre
7 – A, Block R – 3, Muhammad Ali Johar Town, Lahore
Tel: +92 (0)42 35905000 Ext. 4280
Fax: +92 (0)42 35945209
E-mail: crc3@skm.org.pk

2.8.2 Guidelines for Reviewers

You are being asked to evaluate the scientific merit of a research proposal. The institution appreciates your valuable role in this review process. Two weeks before the meeting, you will receive a package containing all of the applications except for those that pose a conflict of interest for you. Included will be a list of applications on which you are expected to focus as a reviewer. It is critical that you promptly alert the SRC (within 48 hours is optimal) to unforeseen conflicts or questionable assignments concerning the matching of your expertise.

Conflict of Interest: The clinical research office will attempt to identify conflicts of interest involving you and any application. Your assistance is necessary. Consider the following as potential conflicts: investigators are listed with whom you have a financial relationship; the funding decision on any application would benefit you directly; you feel there may be a perception of conflict. Notify the SRC in such cases. The SRC will make the final determination after discussion with the medical director (MD). All reviewers will sign a conflict of interest form as a record of their declaration.

Confidentiality: The applications are to be considered confidential, and it is important to respect the privacy of the investigators' ideas. If consultation with an expert is appropriate, contact the secretary SRC who can recruit an outside opinion and secure a signed conflict of interest form.

Expectations of Reviewers : Each application is assigned to at least two reviewers. As a reviewer, you will be expected to write a complete critique.

Amended and Renewal Applications: For revised applications, your critique should include an evaluation of the changes made in response to the last review. You should consider the response by the investigator to the previous criticisms as one component in your overall evaluation of the current application. Note, however, that you are not tied to previous critiques and can raise new criticisms and/or disagree with previous comments on strengths and weaknesses. If the application is a competing renewal, you should include an evaluation of progress over the past project period.

The Written Critique: Consider all aspects of the application. Do not describe the investigator's plans; rather make evaluative statements about the strengths and weaknesses of the proposal. A strong application will contain good ideas, address important issues, and generate confidence that the investigator(s) will make a significant impact. Do not insist on a hypotheses-driven approach if the research is sound and will move the field forward. Focus is important, especially for new investigators. Avoid emphasizing minor technical details, making tutorial comments, or redesigning the investigator's experiments. Put the requirement for preliminary data in perspective such that bold new ideas, young investigators, and risk-taking are encouraged rather than stymied. Be concise; longer reviews are not necessarily better. Sample critiques are less than two (2) pages long. Where possible, try to put the strengths and weaknesses in perspective by indicating their relative magnitude. Do not consider issues outside of scientific merit in your critiques, such as current or past funding levels or personal situations of the investigator.

Scoring: Each scored application is assigned a single, global score (A-E) that reflects the overall impact that the project could have on the field based on consideration of the five review criteria (significance, approach, innovation, investigator, and environment). The emphasis on each criterion may vary from one application to another, depending on the nature of the application and its relative strengths.

Scientific Misconduct: It is vital that you not make allegations of potential misconduct at the meeting or in the critique. Such concerns must be brought to the attention of the SRC in a confidential manner, preferably before the SRC meeting.

Discussion of Applications: The scientific discussion of the proposal will begin with a brief description of the overall goals of the application. Subsequently, reviewers should avoid repeating detailed descriptions of strengths and weaknesses already provided. Identify major issues with which you disagree and raise any issues not brought up previously that you feel should influence the score of the application. It is important that you listen carefully to each presentation and be prepared to defend or change your point of view based on scientific arguments. Keep an open mind, but don't give in just to reach consensus. Do not be afraid to express your view but avoid statements that might be considered offensive. You are strongly encouraged to participate in the discussion of applications not assigned to you. A vigorous discussion involving multiple panel members is ideal.

The consensus is not an absolute necessity, and the chair will decide when further discussion is not likely to resolve scientific differences of opinion. In such cases, it is important to establish the foundation of the disagreement. It is important, however, that you articulate your reasons for assigning a particular score. Consider human subject issues, if any, before scoring. Budget recommendations are addressed after scoring, followed by issues of compliance with regulations and policies regarding animals and biohazards. Please note that, in the event that your views are altered as a result of the discussion, you are encouraged to modify your critique appropriately so that the summary statement reflects your final evaluation of the application.

2.8.3 Review procedures for SRC meetings

The SRC makes recommendations concerning the scientific merit of applications. The specific criteria used to assess the merit of research project applications will vary with types of applications reviewed.

The chairperson of the SRC introduces each application designated for discussion and calls upon the individuals assigned by the SRC to present their evaluations. The assigned reviewers are then called upon for their comments, and group discussion follows. After sufficient discussion has ensued, the chairperson calls for a priority rating to be assigned to the application. Ratings will be assigned by those serving as reviewers of a study who are encouraged not to abstain from assigning a score. Regular members of the SRC can give their feedback about any submitted proposal.

In addition, if there are comments or serious concerns regarding the use of human subjects or animal welfare or biohazards, a motion may be initiated that the application should be coded to reflect these comments or concerns, and an appropriate note will be included in the summary statement.

If additional information is needed before a review group can make a recommendation, a motion for a deferral may be entertained. The review group may, by majority vote, defer an application for additional information, if the information necessary to evaluate the application can be obtained only by visual inspection of the facilities, for a project site visit. Any member may nominate an application for deferral.

2.9 Institutional Review Board

An Independent Hospital Ethical Committee, responsible for reviewing and approving all clinical research projects undertaken at SKMCH&RC or involving hospital patients/patient's data.

The principal duty of the IRB is to safeguard the patient's or test subjects' interest including those identified as vulnerable such as children, prisoners, pregnant women, persons who are mentally disabled, persons who are economically or educationally disadvantaged, and others (e.g. hospital staff) who may be at risk for coercion or undue influence.

It primarily evaluates the ethical aspects of the planned study, and deliberates on a research proposal only after it's scientific content has been validated. The IRB bases its work on principles that have their origin in the Declaration of Helsinki (first written in 1964 & recently at the General Assembly in October 2013) and that are consistent with Good Clinical Practice (GCP) guidelines & applicable regulatory requirements.

The IRB judges:

- The investigator's suitability and prospects for performing the study. Research investigator and the team should be sufficiently qualified by training, education and experience to carry out the study . This is evaluated through a review of the qualification of the principal investigator which are submitted alongside the research proposal.Trial related medical decisions should be made by a suitably qualified physician or physician designee. The investigator may delegate other trial-related duties to other qualified staff such as pharmacist for drug dispensing , nurses for drug administration etc.
- Whether the risks that the patients are being subjected to have been minimized and are proportional to the expected advantages of the results of the study
- Whether the patients are correctly selected and informed about the study.

IRB review is required for any research protocol involving:

1. Patients and users of the SKMCH&RC. This includes all potential research participants recruited by virtue of the patient or user's past or present treatment by, or use of SKMCH&RC. It includes SKMCH&RC patients treated under contracts with private sector institutions
2. Individuals identified as potential research participants because of their status as relatives or carers of patients and users of the SKMCH&RC, as defined above.
3. Access to data, organs or other bodily material of past and present SKMCH&RC patients.
4. Foetal material involving SKMCH&RC patients.
5. The recently deceased in SKMCH&RC premises.
6. The use of, or potential access to, SKMCH&RC premises or facilities.
7. SKMCH&RC staff recruited as research participants by virtue of their professional role. Hospital staff can partcipate in any IRB approved hospital research after eligibility assessment and as per procedures outlined in that protocol.

2.9.1 Terms of Reference

1. At the time of review in a convened meeting a quorum meeting following requirements must be present
    - The IRB must have at least five members.
    - The IRB must include at least one scientist and at least one non-scientist.
    - The IRB must include at least one person who is not affiliated with the institution or in the immediate family of a person affiliated with the institution.
2. The IRB of SKMCH&RC will be composed of at least ten (10) members and

each member will be appointed for a minimum period of two years. The IRB will meet monthly or earlier if needed.

3. IRB members who are affiliated with the institution should maintain minimum of 30% collective participation in IRB review activities however, this would not apply to members who are not affiliated with SKMCH&RC, and serving on IRB on voluntary basis. Participation of affiliated members in IRB is assessed as part of their annual appraisal.
4. Nominations for prospective IRB members are invited from colleagues for both scientist and non-scientist members to serve on IRB, at the time of expansion of IRB membership, which are further reviewed by hospital leadership.
5. A clinical research office member will function as the secretary to the IRB and will assist the principal investigator (PI) & the sponsor in obtaining ethical approval from the IRB.
6. The scientific content of all research projects presented to the IRB must have been validated prior to submission to the IRB.
7. All the necessary documents must be completed and submitted to the secretary to the IRB by the concerned parties at least four weeks prior to the proposed date of the meeting.
8. An IRB processing fee must be submitted to the clinical research office before the meeting. The fee is Rs.30,000 for pharmaceutical sponsored trials and Rs.3,000 for external postgraduate student projects. Undergraduate students and investigator initiated studies by SKMCH&RC staff and are not subjected to an IRB processing fee.
9. The secretary will make sure that final versions of the following documents are sent to all IRB members for review:

   IRB application (Online IRB application can be accessed at link: (https://apps.shaukatkhanum.org.pk:4433/online/irb/index.php)

   - A copy of synopsis along with the attached Scientific Review Committee approval and the IRB approval request
   - study protocol (and any amendments)
   - consent form & subject information sheet both in English & Urdu
   - Study questionnaire/data collection form/interview guide as applicable
   - A copy of the Investigator Brochure and any other available safety information
   - Information about payments and compensation available to subjects
   - The Investigator's current curriculum vitae.
   - Any other documents specifically requested by the IRB
10. After reviewing the above documents, the IRB will issue a letter confirming that it has reviewed the concerned documents (adding the dates & version seen) and outlining its decision with regard to the proposal.
11. During a convened meeting, all IRB members will perform the review of each study and will be expected to
    - explicitly state that, in his/her opinion, the criteria required for approval have been met, and vote (for/against)
    - propose a specific frequency for continuing review
    - carefully describe the proposed conditions or basis for requiring changes or in disapproving research, in cases where approval is not granted
    - IRB decision will be made by majority vote, and voting information will be recorded in meeting minutes

12. Using the above procedures, the IRB may approve, reject, modify or defer any application, pending further information. The decision of the IRB will be conveyed to the principal investigator (PI) and the sponsor and a copy will be retained in the Investigator's Study File & IRB folder.
13. Only those IRB members who are independent of the investigator teams and the sponsor of the study/trial can vote/proffer an opinion on a study/trial-related matter.
14. Only those members who actually participate in the IRB review & discussion can cast a vote/provide an opinion or advice
15. In special circumstances, the IRB can invite non-members with particular expertise for assistance.
16. No subject will be enrolled in any study/clinical trial before the IRB issues its written approval of the study protocol.
17. No deviations from, or changes to, the protocol will be initiated without prior written IRB approval of any proposed amendments, except when necessary to eliminate immediate hazards to the subjects or when the change involves only logistical or administrative aspects of the research projects (e.g. change of the investigator).
18. The investigator will be required to continue to report to the IRB as follows:
    - Periodic progress report (at least annually)
    - Deviation from, or changes to, the protocol designed to eliminate immediate hazards to the study/trial subjects.
    - Changes increasing the risk to subjects and/or affecting the conduct of the study/trial significantly.
    - All adverse events that are serious and/or unexpected.
    - New information that may affect the safety of the subjects or the conduct of the study/trial adversely.
    - The investigator will also inform the IRB if there are any changes to the consent document as a result of any new safety concerns as the participants will need to be re-consented in that case. Any amendment to the informed consent document will be submitted to the IRB for its review and approval prior to its implementation.
19. The secretary to the IRB will be responsible for maintaining all relevant records (e.g., written procedures, membership lists, submitted documents, minutes of meetings and correspondence) for a lifetime period after the completion of the study and make them available upon request from any appropriate regulatory authority(ies). The secretary IRB is also responsible for submitting an annual report of research review activities to the clinical executive board (CEBs) for a review of the research review function.
20. Human subject research involving no more than minimal risk qualifies for exemption. It means that the proposed research activity is exempt from full quorum review by IRB, and no further correspondence is required. A review by IRB chairperson and one of the designated IRB member is required, and it is completed in two to four (2-4) weeks of submission. This type of review is applicable when research involves secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
    (i) The identifiable private information or identifiable biospecimens are publicly

available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects

Investigators should not make final determination that their research is exempt. IRB is an authorized body to make the final determination of exemption.

21. IRB review also ensures that informed consent in research is documented as per GCP requirements and hospital policy on informed consent. A template document outlining requirements for consent in research is available with the clinical research office for investigator use. The investigator should ensure that the following is covered during the process of informed consent for research studies
    - an explanation of the research, duration of patient participation, and procedures to be followed by patients;
    - expected benefits;
    - potential discomforts and risks;
    - alternative treatments and procedures that might also be beneficial;
    - the extent to which confidentiality of records will be maintained;
    - compensation or medical treatments available if an injury occurs;
    - a statement that participation is voluntary;
    - assurance that refusal to participate or withdrawal from participation will not compromise care or access to the hospital's services; and who to contact with questions about the research.
22. A sub-set of research activities may qualify for a waiver of informed consent if it meets following criteria:
    - The research involves no more than minimal risk to subject and involves no procedures for which informed consent is normally required outside of the research context.
    - The waiver or alteration will not adversely affect the rights and welfare of the subjects.
    - The research could not practically be carried out without the waiver or alteration.
    - Whenever appropriate, the subjects will be provided with additional information after participation.
23. Review of application during Pandemics & Public Health Emergencies

    IRB will use its best efforts to continue to function during a pandemic. It will provide a rapid but robust review. IRB will adapt to meet by video conferencing and accept online reviews (in place of signed forms)

    IRB will further ensure that practical and meaningful consent process is in place for patients affected by diseases outbreak. If appropriate, alterations in the informed consent process, including waiver of informed consent and verbal consent can be approved by IRB.
24. To obtain an application template, guidelines for IRB approval and for any further information regarding IRB approval, please contact:

    Clinical Research Administrator
    Shaukat Khanum Memorial Cancer Hospital & Research Centre
    7 – A, Block R – 3, Muhammad Ali Johar Town, Lahore
    Tel: +92 (0)42 35905000 Ext. 4280

Fax: +92 (0)42 35945209
E-mail:crc3@skm.org.pk

2.9.2 Guidelines for IRB reviewers:

Criteria for IRB Approval of Research

Institutional Review Board (IRB) is responsible for reviewing and approving all Clinical Research Projects undertaken in the hospital or involving the hospital's patients or patient data.

The principal duty of the IRB is to safeguard the welfare of patients who participates in research (participants). It primarily evaluates the ethical aspects of the planned study.

The IRB judges that the investigator is suitable to conduct this research (sufficiently qualified and experienced), and ensures that the rights of study participants are protected from possible risks of research.

In order to approve research under review, IRB should determine that all of the following requirements are satisfied

1. Risks to subjects are minimized by using:
   i) procedures consistent with sound scientific design and which do not unnecessarily expose subjects to risk
   ii) whenever appropriate by using procedures already being performed on subjects for diagnostic or treatment purposes
2. Risks to subjects are reasonable in relation to the anticipated benefits
3. Selection of subjects is equitable (Are these participants appropriate to the research question)
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative
5. Informed consent will be appropriately documented
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
7. When appropriate, there are adequate protections to protect the privacy of subjects and to maintain the confidentiality of data.

Note: When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as hospital staff, children, prisoners, pregnant women, mentally disabled, or economically or educationally disadvantaged persons, IRB should ensure that appropriate safeguards have been included in the study to protect the rights and welfare of these subjects. In cases where research involves the participation of hospital employees, IRB should ensure that mechanisms are in place to obtain voluntary participation and appropriate confidentiality. Informed consent must state that refusal to participate will not result in any loss of privileges or negative impact on evaluation.

2.9.3 Investigator Responsibilities and Responsible Conduct of Research

As per ICH-GCP, all researchers involved in research must ensure the following as part of responsible conduct of research

- The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the research
- The investigator should be thoroughly familiar with the research protocol, should be aware of, and should comply with, GCP and the applicable regulatory requirements.
- The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority (ies) where applicable.
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- The investigator should ensure availability of adequate resources for conducting a research study such as adequate time allocation to research activities, qualified and trained staff as members of research team and other logistics as per study need.
- The principal investigator of a study has ultimate responsibility for maintaining study oversight (including but not limited to ensuring protocol compliance, investigational products accountability) and for supervising any individual or party to whom the investigator delegates trial-related duties and functions.
- A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
- During and following a subject's participation in a trial, the investigator should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial.
- The investigator is responsible for ongoing ethics and regulatory communication as applicable with relevant committees following initial approval of the study.
- Investigators are responsible for obtaining and documenting informed consent from research participants as per approved protocol consent procedures. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Neither the investigator nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial. Once consent has been obtained, research participation should be clearly recorded in the research subjects' hospital records, and a copy of the signed consent must be retained in the research files.
- The investigator should maintain adequate and accurate source documents and research related records.
- The investigator should submit written summaries of the trial status to the IRB at least annually, or more frequently, if requested by the IRB.
- All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting.
- If a clinical trial is prematurely terminated or suspended for any reason, the investigator should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority (ies).
- Upon completion of the research study, the investigator, where applicable, should inform the IRB with a summary of the trial's outcome, and the regulatory authority (ies) with any reports required.
- For research projects undertaken as part of training requirements, following are the supervisor responsibilities for oversight of such research activities

- Supervisor to only allow project initiation once IRB approval is confirmed and should conduct regular project update meetings
- Promptly notify the institution in case of any research misconduct which may lead to suspension of the study or termination of ethics approval for that study.

3. AUTHORSHIP

3.1 Acknowledging Contributions

Authorship is an explicit way of assigning responsibility and giving credit for intellectual work. The two are linked. Authorship practices should be judged by how honestly they reflect actual contributions to the final product. Authorship is important to the reputation, academic promotion, and grant support of the individuals involved as well as to the strength and reputation of their institution.

Many institutions, including medical schools and peer-reviewed journals, have established standards for authorship. These standards are similar on basic issues but are changing over time, mainly to take into account the growing proportion of research that is done by teams whose members have highly specialized roles.

In practice, various inducements have fostered authorship practices that fall short of these standards. Junior investigators may believe that including senior colleagues as authors will improve the credibility of their work and its chances of publication, whether or not those colleagues have made substantial intellectual contributions to the work. They may not want to offend their chiefs, who hold substantial power over their employment, research opportunities, and recommendations for jobs and promotion. Senior faculty might wish to be seen as productive researchers even though their other responsibilities prevent them from making direct contributions to their colleagues' work. They may have developed their views of authorship when senior investigators were listed as authors because of their logistic, financial, and administrative support alone.

Disputes sometimes arise about who should be listed as authors of an intellectual product and the order in which they should be listed. When disagreements over authorship arise, they can take a substantial toll on the goodwill, effectiveness, and reputation of the individuals involved and their academic community. Many such disagreements result from misunderstanding and failed communication among colleagues and might have been prevented by a clear, early understanding of standards for authorship that are shared by the academic community as a whole.

Discussions of authorship in academic medical centres usually concern published reports of original, scientific research. However, the same principles apply to all intellectual products: words or images; in paper or electronic media; whether published or prepared for local use; in scientific disciplines or the humanities; and whether intended for the dissemination of new discoveries and ideas, for published reviews of existing knowledge, or for educational programs.

Although authorship practices differ from one setting to another, and individual situations often require judgment, variation in practices should be within these basic guidelines.

3.2 Authorship Guidelines

1. Everyone who is listed as an author should have made a substantial, direct, intellectual contribution to the work. For example (in the case of a research report) they should have contributed to the conception, design, analysis and/or interpretation of data. Honorary or guest authorship is not acceptable. Acquisition of funding and provision of technical services, patients, or materials, while they may be essential to the work, are not in themselves sufficient contributions to justify authorship.

2. Everyone who has made substantial intellectual contributions to the work should be an author. Everyone who has made other substantial contributions should be acknowledged.

3. When research is done by teams whose members are highly specialized, individual's contributions and responsibility may be limited to specific aspects of the work.

4. All authors should participate in writing the manuscript by reviewing drafts and approving the final version.

5. One author should take primary responsibility for the work as a whole even if he or she does not have an in-depth understanding of every part of the work.

6. This primary author should assure that all authors meet basic standards for authorship and should prepare a concise, written description of their contributions to the work, which has been approved by all authors.

3.3 Order of Authorship

Many different ways of determining the order of authorship exist across disciplines, research groups, and countries. Examples of authorship policies include descending order of contribution, placing the person who took the lead in writing the manuscript or doing the research first and the most experienced contributor last and alphabetical or random order. While the significance of a particular order may be understood in a given setting, the order of authorship has no generally agreed-upon meaning.

As a result, it is not possible to interpret from the order of authorship the respective contributions of individual authors. Promotion committees, granting agencies, readers, and others who seek to understand how individual authors have contributed to the work should not read into the order of authorship their own meaning, which may not be shared by the authors themselves. The authors should decide the order of authorship together.

Authors should specify in their manuscript a description of the contributions of each author and how they have assigned the order in which they are listed so that readers can interpret their roles correctly. The primary author should prepare a concise, written description of how the order of authorship was decided.

3.4 Implementation

Research teams should discuss authorship issues frankly early in the course of their work together. Disputes over authorship are best settled at the local level by the authors themselves or the laboratory chief.

If local efforts fail, the medical director (MD) can assist in resolving grievances. Laboratories, departments, educational programs, and other organizations sponsoring scholarly work should post, and also include in their procedure manuals, both this statement and a

description of their own customary ways of deciding who should be an author and the order in which they are listed. They should include authorship policies in their orientation of new members.

These policies should be reviewed periodically because both scientific investigation and authorship practices are changing.

4- SKMCH&RC CLINICAL RESEARCH FUND

The aim of the fund is to provide mini-grants to encourage and support budget requirements for research activities at SKMCH&RC.

4.1 Applying for Funds

Eligibility: Any investigator based and conducting research at SKMCH & RC. The research project must have approval from the SRC and IRB.

Eligible expenses: Research equipment (machines), materials (chemicals, glassware), and services, travel grants for specialist training for research. No salary or stipends are allowed.

Application Process: Investigators need to complete an application outlining their requirements with justification. The application must be accompanied by approval documentation from the SRC and IRB, no more than two pages and with an itemized budget.

Review Process: The clinical research office has primary responsibility for reviewing applications and making recommendations to the Medical Director (or designee, in applications where a conflict of interest exists). Awards will be announced within two weeks of the application deadline.

Award Disbursement: Funds remaining at the end of the project will revert back to the Research Fund to be used for subsequent mini-grant awards. Awards cannot be transferred to any other person or project.

Expectations: After disbursing the award and once the project starts, the investigator will be required to submit periodic budget expenditure reports. Clinical research office will communicate with investigators to collect these reports, which will be reviewed by the medical director.

5- GUIDELINES FOR UNDERGRADUATE & POSTGRADUATE RESEACH

5.1 Requirements

- The student must be registered at a recognized University in an undergraduate or p ostgraduate program at the time of submission of the research proposal.
- An official college transcript and one letter of recommendation from your college supervisor addressed to:

  Clinical Research Administrator
  Shaukat Khanum Memorial Cancer Hospital & Research Centre
  7 – A, Block R – 3, Muhammad Ali Johar Town, Lahore
  Tel: +92 (0)42 35905000 Ext. 4280/4286
  Fax: +92 (0)42 35945209
  E-mail: crc3@skm.org.pk/crc@skm.org.pk
- Completion of an online submission form available on the SKMCH & RC website. The form requires a three-hundred (300) word abstract describing the research; including objectives, setting, study design, and anticipated duration of stay/work at SKM.

- In addition, protocol synopsis and related documents such as consent forms, case report forms etc. should be submitted at least five (5) months before the research deadline to allow adequate time for approvals.

5.2 Procedure

- Once the clinical research office receives the abstract and protocol synopsis, these will be placed on an internal list of projects. The list is for consultants, and other SKM staff to view and select projects for supervision. If the project is selected, the student will be informed within four weeks. If after four weeks, the project has not been selected, it will be removed from the list, and the student will be informed that the project was not accepted.

- The project supervisor will assist the student in satisfying the requirements of the Research Guidelines at SKMCH & RC, and in assigning role and responsibilities to each investigator involved in the study, and accordingly clarifying authorship clauses.

- The project must initially be submitted to the Scientific Review Committee (SRC), where the technical and scientific content of the project will be reviewed (refer to Research Guidelines section titled "Ensuring Good Clinical Practices").

- If the research involves humans (including surveys or interviews), the researcher must obtain official approval from the hospital's Institutional Review Board (IRB), please refer to Research Guidelines section titled "Ensuring Good Clinical Practices" for further details. Postgraduate students are required to pay an IRB processing fee of Rs.3, 000.

- The SRC and IRB process for each protocol is slightly different (dependent on ethical issues inherent to research methodology, subject population, research question, etc.) and may take around three months for final approval, provided no major changes are necessary. Clarification and revisions to original submissions are common and are handled as quickly and efficiently as possible.

- Understanding the issues and receiving proper guidance and supervision in the crafting of both the research study and the ethical protocol can minimize turn-around time.

- Proposals will be reviewed on an ongoing basis. It is expected that decisions will be made within three months, following receipt of the proposal.

- Written approval from the SRC and IRB will be sent to the medical director (MD), and the student may commence the project once he/she has received an official approval letter from the research office.

5.3 Application Form

In addition to the information below you must send an official college transcript and one letter of recommendation from your college supervisor addressed to:

Clinical Research Administrator
Shaukat Khanum Memorial Cancer Hospital & Research Centre
7 – A, Block R – 3, Muhammad Ali Johar Town, Lahore

Tel: +92 (0)42 35905000 Ext.4280/4286
Fax: +92 (0)42 35945209
E-mail: crc3@skm.org.pk/crc@skm.org.pk

Personal Information
Last Name
First Name
Date of Birth
University/College
Degree Title
Year of Graduation
Institutional Supervisor, Designation
Contact Information
Email
Telephone Number
Address

Abstract (300 words maximum)

The following subheadings have been provided; you may use these or alternatively submit an abstract which includes this information.
Title
Introduction
Objectives
Setting
Subjects
Study Design / Analysis
Expected duration of stay/work at SKMCH&RC

6- GUIDELINES FOR RESEARCH COLLABORATIONS & GRANT APPLICATIONS

Following are important considerations to be followed while undertaking research collaborations between SKMCH&RC and collaborating academic groups, organizations and sponsors of research

6.1 Compliance to research guidelines

Research guidelines define the scientific standard and code of ethical conduct of research involving human subjects, which should be followed by all researchers of the hospital, as well as collaborating institutes and individuals.

6.2 Feasibility assessment

This is a process to assess if proposed collaboration is feasible in SKMCH&RC before the expression of interest can be communicated. It is usually done with the help of related specialists who can take the lead and play a key role in the conduct of the proposed research. Medical director as head of research is kept posted for information and approvals. At this step, we are interested to see if we are in agreement with the scientific content of the proposed research and have sufficient resources to perform it (investigators, availability of target population and recruitment potential, other facilities, time requirements and funds). At this point, any major ethical concerns raised by the subject area experts are also discussed with the proposed collaborator. For collaborative research projects, a designated person from SKMCH&RC must be part of the proposed project.

Mandatory approvals and legal agreements

Research studies to be done in collaboration with other organizations would require additional steps which may involve IRB review at collaborating institute, collaboration agreement or data/material transfer agreement and funding agreement, or others as per relevant national and international laws and regulations.

6.3 Grant applications

After initial feasibility assessment completion, the collaborating partners may proceed with a grant application with an undertaking that the proposed project will be initiated upon successful receipt of the grant funds as per SKMCH&RC requirements for the ethical conduct of research and applicable local and international regulations. Clinical research office facilitates prospective collaborators in this process

For further details please contact the following

Clinical Research Administrator
Shaukat Khanum Memorial Cancer Hospital & Research Centre
7 – A, Block R – 3, Muhammad Ali Johar Town, Lahore
Tel: +92 (0)42 35905000 Ext.4280/4286
Fax: +92 (0)42 35945209
E-mail:
crc3@skm.org.pk/crc@skm.org.pk

6.4 Guidelines for Collaborating groups, Organizations and Sponsors and for use of Contract Research Organization (CROs) by Sponsors

In line with its commitment to perform research of highest scientific and ethical standard, Hospital leadership ensures that collaborating groups, organizations and sponsors ensure their compliance to the ethical values and processes promising protection of human research participants from research risk.

It is a pre-requisite that all collaborators declare their commitment to the professional and ethical conduct of research. This declaration must be signed by collaborator's authorized signatory before the start of any collaborative study in SKMCH&RC.

(A template declaration is provided below)

Declaration Template

Subject: Declaration confirming commitment to ethical conduct of research

Reference of collaboration (provide complete name of collaborative group and title of study):

I, the undersigned (name and position), and representative of (full name of the collaborator group), and proposing collaboration (title), confirm that:

- I will comply with the hospital's policies and processes for monitoring and evaluating the quality, safety, and ethics of the research
- I will use research teams that are appropriately trained and qualified to conduct the research
- I will protect the privacy and confidentiality of subject data
- I will not permit patient or researcher incentives that would compromise the integrity of the research
- I will ensure that the research data are reliable and valid, and the results and reporting are statistically accurate, ethical, and unbiased.
- Furthermore, when sponsors plan to use a contract research organization they will ensure the following
- I will share information and documentation related to the activities and responsibilities assigned to a contract research organization.
- I will ensure that duties and functions transferred to the contract research organization are contained in a written contract, which should specify that the contract research organization or sponsor is responsible for monitoring and evaluating the quality, safety, and ethics of the research.
- I will be responsible for monitoring the above contract.

Signed:_____

Name:_____

Designation:_____

Affiliation:_____

PROCESS TO GET IRB APPROVAL

This section contains information on the process to get approval from Institutional Review Board (IRB) for research studies qualifying for full quorum review as well as for exemption.

1.0 UNDERSTANDING WHEN IRB REVIEW IS NEEDED

Every research activity involving human subjects needs prior approval from IRB before it can be initiated at SKMT. Every investigator should determine

- Whether an activity is research **AND** involves human subjects that must be reviewed by an IRB
- Whether it needs a review by the full quorum IRB **OR** the proposed activity is exempted from full quorum review

1.1 Is My Project Human Subject Research?

This section provides guidance to investigators who may be uncertain if their study meets the definitions of human subject research. The guidance provided here is general and may not be specific enough for particular situations.

1.1.1 Human subjects research

The first question a researcher should consider with respect to IRB review is whether the research project fits the definition of human subject research. Following definitions will help in making this determination

1.1.2 Defining research

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
Audits and service evaluations also employ systematic and rigorous methods, but these differ from research in that audit seeks to measure existing practice against evidence-based standards, and service evaluation addresses local service issues. It is noteworthy to understand audits done for quality assurance purposes are different from clinical audits and outcome research.

1.1.3 Defining human subjects

1.1.3.1 A **"human subject"** is defined as, "a living individual about whom an investigator obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information."

1.1.3.2 The definition extends to the use of human organs, tissue and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.

1.1.4 "Living individual" – "The specimen(s)/data/information must be collected from live subjects."

Specimens/information from subjects now deceased may not be human subjects.

1.1.5 **"About whom"** – "a human subject research project requires the data received from the living individual to be **about** the person."

1.1.6 **"Intervention"** – "includes physical procedures, manipulations of the subject, or manipulations of the subject's environment for research purposes."

1.1.7 **"Interaction"** – "includes communication between the investigator and the subject. This includes face-to face, mail, and phone interaction as well as other modes of communication."

1.1.8 **"Identifiable private information"** – "includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation is taking place," and "information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, medical record)."

1.1.9 **"Identifiable"** – means the information contains one or more data elements that can be combined with other reasonably available information to identify an individual (e.g. Medical Record Number).

1.1.9.1 Studies based on data that are individually identifiable but are also publicly available may not constitute human subjects research. However, the term "publicly available" is intended to refer to record sets that are truly readily available to the broad public, such as cancer statistics data, or federal health or educational statistics.

1.1.9.2 An investigator should not assume information qualifies as "publicly available" merely because it has been posted on an electronic website and can be accessed without authorization.

1.2 What type of IRB review is needed?

This section provides guidance to investigators to understand and determine what type of IRB review may be needed for their research project so that investigators can prepare IRB submission accordingly. IRB will finally determine what type of review is needed for a certain activity after having a look at the research project. Two common types of review are:

1.2.1 Exemption

Human subject research involving no more than minimal risk qualifies for exemption/grant of exempt status. It means that the proposed research activity is exempt from full quorum review by IRB, and no further correspondence is required. A review by IRB chairperson, and one of his designees is required and it is completed in two to four (2-4) weeks of submission. This type of review is applicable for secondary research uses of identifiable private information or identifiable bio specimens, if at least one of the following criteria is met:
(i) The identifiable private information or identifiable bio specimens are publicly available;
(ii) Information, which may include information about bio specimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be

ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects
(Please see decision chart)
Investigators should not make final determination that their research is exempt. IRB is an authorized body to make the final determination of exemption.

1.2.2 Full quorum review

If your activity is a research & involves living individuals about whom an investigator obtains

- data through intervention or interaction with the individual, or
- identifiable private information

(Please see decision chart)
It would require a full quorum review by IRB in a convened meeting with a quorum present.
The studies should secure a prior Scientific Review Committee (SRC) approval.

1.3 Does case report require IRB review?

A case report is a retrospective analysis of a case, to develop information to be shared for medical/educational purposes. If an investigator wishes to make a publication of case report, it should be reviewed by IRB. One designated IRB member and Chair IRB will review case report to assess that

i. It meets the definition of a case report,
ii. Appropriate informed consent has been obtained from the participant,
iii. Authors have anonymized the patient's details as much as possible and it does not contain any direct or indirect identifiers to allow information to be used alone or in combination with other information to identify an individual who is a subject of the information.
iv. If the patient is deceased, the authors must obtain consent from adult next of kin.
v. In case, it is not possible to obtain informed consent, authors should provide a reasonable justification for waiver of informed consent and must ensure that exhaustive attempts have been made to contact the patient/family. Authority to grant waiver of informed consent lies with IRB.
vi. Case report manuscript should not contain any illustrations which may lead to identification of participant

In writing a case report, collaboration among all the health care professionals (involved in care of the proposed case) should be encouraged. All authors must have made an individual contribution to the writing of the article and not just been involved with the patient's care. This practice is associated with significant increase in quality of publication and can prevent duplicate publication.

In order to prevent duplication in publication of case reports, a database of medical record numbers of cases reported in case reports has been established and can be accessed at given link (https://apps.shaukatkhanum.org.pk:4433/online/irb/index.php). Authors must consult this database to ensure that no duplicate publication is carried out.

Same data set may be used to prepare more than one case report reflecting on different aspects of the case in interest. However, an assessment by Medical Director will be carried out, in cases where duplicate publication is suspected or where two publications are of a similar nature. In case of a conflict, final decision will be made by the medical director.

2.0 HOW TO PREPARE FOR IRB

For making IRB submission, investigators should submit the following documents.

i. IRB application
ii. Research synopsis
iii. Informed Consent Form (English & Urdu version) for patients, if applicable
iv. Informed Consent Form (English & Urdu version) for healthy controls, if applicable
v. Questionnaire/Clinical data collection forms/interview guide as applicable, if applicable
vi. Itemized budget with the indication of the source of funding
vii. A copy of the Investigator Brochure and any other available safety information
viii. Information about payments and compensation available to subjects
ix. The investigator's current curriculum vitae
x. Conflict of interest declaration
xi. Collaborator/Sponsor/Contract Research Organization undertaking (as applicable)
xii. Material Transfer Agreement/Collaboration Agreement/Indemnity Insurance documentation, where applicable
xiii. Waiver of informed consent (provide written justification for waiver request)

2.1 Prepare your study documents

IRB application form and other templates are listed below to help you prepare your study documents.

2.1.1 IRB application Form
2.1.2 Online IRB application can be accessed at link: https://apps.shaukatkhanum.org.pk:4433/online/irb/index.php)
2.1.3 Template research synopsis
2.1.4 Template for developing informed consent (English-Urdu)
2.1.5 Template for developing informed consent for case report (English-Urdu)
2.1.6 Case report Exemption assessment form
2.1.7 Research study budget sheet
2.1.8 Collaborator Ethical Undertaking

3.0 MAINTAINING YOUR IRB APPROVAL

After IRB approval, you would need to maintain approval conditions. For this purpose, you would need to continue to correspond with IRB in following cases

3.1 IRB Continuing Review Report
3.2 IRB Study Close Out Report
3.3 Amendment (changes in study protocol)

If you wish to make any amendments in research study which is already IRB approved, kindly submit amendment request form and a letter addressing chairperson IRB, summarizing the proposed amendments. Also include in your letter, how it can affect study risk-benefit ratio. Also, submit a revised proposal incorporating the amendment. In case the risk benefit ratio is affected by the amendment, IRB may seek further information or documents, as appropriate.

3.4 Notifications of adverse events

Adverse events/Serious Adverse Events should be reported using following forms:
Adverse Event Reporting Form

Shaukat Khanum Memorial Cancer Hospital and Research Centre

Document Change Request

R/CEN/QPS-002/v.2

Originator: Dr. Saima Faisal	**Department:** Clinical Research Office (CRO)	**Date:** 30-04- 2025
Document #: **POL/A/CEN/CRO-001/v.5**	**Document Name:** Research Guidelines	**Version #:** 05

Reason for change:

1- Change in process

2- Compliance with JCIA HRP standards

Nature of change:

1- Hyperlinks updated in Process to get IRB.

2- Addition and numbering of forms in 2.1 Preparer your study documents

3- Addition of Amendment request form in 3.3 .

Any resources needed: No	**Allocation or Reallocation of responsibilities and authorities:** Same as previous

Minutes of Review Committee:

Review of the document was carried out over emails and finalization of the draft has been completed thereafter.

- **Change Approved** **YES**
- **Change Disapproved**

Reason if disapproved: Not applicable.

Prepared by: Farah Asif Dr.	**Approved by:** Chief Medical Officer (CMO)
Approval Date: April 2025	**Version No. of document after change:** Version 6