MINISTRY OF HEALTH

GENERAL ADMINISTRATION FOR RESEARCH AND STUDIES

RESEARCH PROPOSAL SUBMISSION MANUAL

(2015/1436)

Index

ACRONYMS

AE:	Adverse Event.
ADR:	Adverse Drug Reaction.
CDP:	Concept Development Paper.
Co-PI:	Coordinating Principal Investigator
GDRS:	General Directorate for Research & Studies
DSA:	Data Share Agreement
DG-GDRS:	Director General - General Directorate for Research & Studies.
DPI:	Deputy Principal Investigator.
EC:	Ethical Committee
FFR:	Final Financial Reports
FTR:	Final Technical Report
GCP:	Good Clinical Practice
HA:	Higher Authority
IB:	Investigator's Brochure
IRB:	Institutional Review Board
ITC:	Internal Technical Committee
KACST:	King Abdulaziz City for Science and Technology
NCBE:	National Committee of Bioethics
NDA:	Non-Disclosure Agreement
NIH	National Institutes of Health
NSTIP:	National Science, Technology and Innovation Plan
PFRs:	Periodic Financial Reports
PI:	Principal Investigator
PM:	Project Manager
PTR:	Periodic Technical Report
RPAC:	Research Priorities Adoption Committee
RP:	Research Proposal
RPPR	Research Performance Progress Reports
SC:	Scientific Committee
SFDA:	Saudi Food and Drug Authority
SOPs:	Standard Operating Procedures.
WHO:	World Health Organization

GLOSSARY

- Adverse Event (AE):

Any unwanted medical occurrence during treatment with a study drug that does not necessarily have a relationship with the treatment being given.

- Adverse Drug Reaction (ADR):

A noxious and unintended response to a medicinal product at doses normally used in human for prophylaxis, diagnosis or therapy.

- **Bylaw:**

A list of rules and regulations enacted by the Ministry of Health to provide a framework for its operation and management of health researches conducted in its facilities. Also, bylaw may specify the qualifications, duties, rights, and liabilities of MOH stakeholders.

- **Clinical Trial (CT):**

Any research study that prospectively assigns human participants to one or more health-related interventions to answer specific questions about biomedical or behavioral interventions, including new treatments (such as novel vaccines, drugs, dietary choices, dietary supplements, and medical devices) and known interventions that warrant further study and comparison.

- **Confidentiality:**

Preserving authorized restrictions on access and disclosure, including means for protecting personal and medical information of human research participants enrolled in biomedical, behavioral, clinical and other forms of health research and studies.

- **Consultant:**

Is an experienced individual having a distinct qualifications and a long experience in his career that can provide the best consultancy services to health research team

to help them for making the best possible choices. The consultant should have at least a doctorate degree or its equivalent.

- **Coordinating Principal Investigator (Co-PI):**

Is a co-director of the project, sharing leadership responsibilities with the PI. In some situation particularly with multi-site projects, more than one individual is considered as responsible for administrative, financial, and scientific conduct of the project. The Co-PI should have at least a doctorate degree or its equivalent.

- **Deputy Principal Investigator (DPI):**

A scientific and technical qualified individual who will be expected to take the lead in research project and running the research's workload in case of unavailability of the PI. DPI is hierarchically directly below the PI.

- **Field Auditor** (Internal Quality Assurance Specialist):

A scientifically qualified person and has a practical experience that responsible for the day-to-day execution of project, to make sure its compliance with the approved proposal and its commitment to scientific integrity and ethical regulations.

- **General Directorate for Research and Studies (GDRS):**

Is the authorized directorate in the Ministry of Health (MOH) to provide the infrastructure, resources, guidelines, management services and leadership needed to promote high quality health researches to improve health.

- **Grant:**

Is a financial support provided by MOH to its stakeholders within a contract, to conduct a specific research or creative work according to MOH regulations.

- **Health Research:**

Is a creative work undertaken on a systematic basis in order to generate high quality knowledge that can be used to promote, restore and improve health.

- **Higher Authority (HA)**:

  Is the MOH's official to whom the GDRS reports.

- **Internal Technical committee (ITC)**:

  A scientific expert committee, within the GDRS-MOH, that is responsible for reviewing and evaluating research proposals.

- **Investigator's Brochure (IB):**

  A collection of all clinical and non-clinical data on the investigational product(s).

- **Principle Investigator (PI):**

  Is a scientific and technical qualified person who is responsible for designing, execution, and management of a research project in compliance with MOH guidelines. The PI should have at least a doctorate degree or its equivalent.

- **Research Priorities Adoption Committee (RPAC)**:

  A higher supervisory committee to study and adopt the research plans and health research priorities, which has been approved by the scientific committee.

- **Project manager (PM):**

  Is a professional in the field of project management who has primary responsibility for the management, financial aspects and closing of the research project.

- **Research Associate:**

  Is a person who supports a research project under a principle investigator and usually possesses a post-graduate level education (Masters/PhD).

- **Research Assistant:**

  Scientifically qualified persons can help in implementation of work tasks, conduct experiments, and get the results according to approved proposal, under the direct supervision of research team. They include technicians, professionals (physicians, nurses, Pharmacists, engineers, ….), Administrators, financial and others.

- **Research Ethics Committee (ET):**

  An independent review committee comprising of medical, scientific and non-scientific/non-medical members, whose responsibility is to verify the protection of the rights, safety and well-being of human subjects involved in the study.

  Research proposal (RP):

  Is a document that provides a detailed description of the proposed research program. It should outlines the entire research process from beginning to end and may be used to request financing for the project.

- **Research Team:**

  Are the qualified persons responsible for conducting health research. It includes both head researcher and the research associates.

- **Reviewer:**

  Is an experienced individual having a distinct qualifications and a long experience in his career that can provide scientific and ethical review for scientific papers, research proposals, follow-up project's reports and other scientific products.

- **Saudi Food and Drug Authority (SFDA):**

  Is an independent body to regulate, oversee, and control food, drug, medical devices, as well as to set mandatory standard specifications thereof, whether they are imported or locally manufactured.

- **Scientific Research Review Committee (SC)**:

  A scientific expert committee consists of a group of experienced individuals that are responsible for the peer review of the MOH scientific work programs, research and studies. Also, it is responsible for setting health research priorities. It reports to the Priorities Adoption Committee.

INTRODUCTION:

WHO framework sets out to delineate a boundary of the health research system based on the following definition: "The people, institutions, and activities whose primary purpose is to generate high quality knowledge that can be used to promote, restore, and or maintain the health status of populations". It can include the mechanisms adopted to encourage the utilization of research *(WHO, 2001)*.

The main goals of health research are the advancement of scientific knowledge and utilization of knowledge to improve health and health equity. There are many intermediary benefits, such as knowledge benefits, benefits to future researchers, political and administrative benefits, benefits to the health sector, and broader social and economic benefits. Nevertheless, the intrinsic goals of health research, as opposed to other research or activities, should ultimately contribute to improvements in health and health equity *(WHO, 2001)*.

Health research supports health systems in the delivery of better, fair and equitable health care to all people. Also, health research should serve as a driver for health policy and practice. It does so by identifying health problems and providing the suitable solutions *(WHO, 2012)*.

The General Directorate for Research and Studies (GDRS) has a vital role in planning, management, and supervising health research in the Ministry of Health (MOH). This is only possible if policies, guidelines, and procedures about health research are well crafted. Consequently, the stakeholders and researchers should have an easy access to those guidelines through an electronic website. The research guidelines certainly streamline the smooth submission, funding, implementation, follow-up and publication of the research within the ethical framework together with scientific integrity. The research guidelines support health research initiatives in the Kingdom of Saudi Arabia (KSA), with a focus both on promoting health research as a tool for national development and further help develop national research programs. Also, the research guidelines facilitate the use of evidence-based information both for policy formulation and health planning for provision of quality health care services and prevention of diseases *(WHO, 2011)*.

The GDRS is dedicated to advancing and ensuring the development and application of appropriate guiding standards for MOH researchers and stakeholders by supporting and facilitating the management of health research through a clear and restrictive guiding manual.

This giding manual intend to assist researchers undertaking biomedical, public health or clinical research involving MOH participants or research on issues relevant to Saudi health. This version provides a guidance for MOH researchers and stakeholders to promote the design, submission, implementation and monitoring of high quality health research projects. It is expected that all those who undertake research involving MOH will read these guidelines prior to making a submission of their research proposals to GDRS.

Vision, Mission, Values and Objectives of the GDRS-MOH to Promote and Support Health Research in MOH:

Vision:

To be recognized nationally, regionally and internationally as a leading center for both basic and applied health research.

Mission:

To provide the infrastructure, resources, guidelines, and leadership needed for MOH stakeholders to promote and sustain high quality health researches, education, training, and community outreach to improve health.

Values:

The GDRS promotes equitable and sustainable health developments across the Kingdom following the standard scientific and ethical principles:

Accountability:

GDRS is responsible for the achievements and successes of health research to develop health care services.

Teamwork:

GDRS cooperates with other national and international health research bodies and is committed to the overall national health research objectives and agendas.

Integrity:

GDRS guidelines demonstrate honest scientific and ethical framework coupled with a high moral standards widely trusted and culturally respected.

Leadership:

GDRS as a representative of MOH understands, accepts and supports the health research and fosters values consistent with the aforesaid mission in the KSA.

Collaboration:

Collaboration with other health community partners and stakeholders for different health problem issues.

Respect:

We foster an environment of mutual respect and trust amongst ourselves and with all whom we serve**.**

Excellence:

We are committed to achieving the highest level of excellence in conducting basic and applied health researches.

General Objective:

GDRS by developing comprehensive health research guidelines manual is geared to promote sustainable and efficient health care services for Saudi peoples using evidence-based data derived from research in health.

Specific Objectives:

1. Promote the concept of health research in MOH.
2. Facilitate, promote and support the conduction of high quality health research in MOH.
3. Increase the number of MOH researchers conducting basic and clinical health research to eliminate health disparities
4. Generate knowledge and solutions relevant to the national health priority problems.
5. Help the healthcare providers in making decisions by delivering accurate and valid evidence based health data.
6. Promoting and disseminating the results of health researches to encourage their contribution to health science.
7. Promote health research capacity building for MOH stakeholders.

Instructions for Conducting MOH Health Research Projects

Types of health research proposals authorized by the Ministry of Health (RPs):

1. Funded RP
2. Non-funded RP.

1- Concept Development Paper (CDP):

CDP is a preliminary pre-proposal step aiming to clarify and organize the proposed ideas in a short written form (one or two pages) to be reviewed before submission of the formal proposal. The CDP can save time and effort for both the reviewing agencies and the researchers.

Concept Development Process:

- The Principle Investigator (PI) should submit his CDP to the GDRS through the e-portal of the MOH (www.moh.gov.sa) using the approved form, for a preliminary approval before the submission of a complete RP.
- The CDP should cover a summary (up to 300 words) including the following issues:
  - Background.
  - Objectives.
  - Material and methods.
  - Expected results.
  - Value to MOH.
- The CDP should match one of the research priorities of MOH.
- The Internal Technical Committee (ITC) in the GDRS will review CDP.
- If the submitted CDP is accepted, an approval letter will be sent to PI through his official email within 7 working days, and then the PI should submit a completed proposal form, within 14 working days.
- If the PI does not respond within the previously assigned period, his CDP may be excluded.

2- Guidelines for Research Proposal Submission:

2.1: Requirements for Proposal Submission:

- A cover letter from the principal investigator (PI) to the DG-GDRS. The cover letter must contain the following data:
  - Name of the (PI) and research associates.
  - Research title both in Arabic and in English languages.
  - PI civil or Eqama ID number for research submission.
  - PI civil ID number for postgraduate degrees.
  - PI telephone & mobile number.
  - PI e-mail address.
  - Name and address of health research conducting sites.
- NIH certificate for PI and research team.
- PI affiliation institution letter.
- CV of the PI and all research team members (each CV should not more than 3 pages).
- An approval letter of the research proposal from a registered MOH ethics committee.
- Other documents:
  - Letter from the supervisors of undergraduate and post-graduate university students.
  - Letter from the cultural attaché [only for fellowship students enrolled in universities abroad KSA].
- Any other essential documents required by GDRS.

2.2: General Instructions for Proposal Submission:

2.2.1: For All Types of Research Proposals (either funded or non-funded):

a. The MOH stakeholders can be participated to conduct health researches as principle investigators, research associates, other research team members, consultants or reviewers, according to their qualifications and experiences,

regarding that these participation does not conflict with their original duties.

b. The MOH has the right to request, from health research experts (researchers or entities), to prepare a research project of high scientific merit and according to MOH health research priorities.
c. The research team especially the PI must read the manual for the technical, financial and administrative guidelines before starting to fulfill the application form.
d. The application form should be fulfilled and submitted electronically through the GDRS webpage.
e. The proposal should be submitted only by PI using the approved application form.
f. The duration of the project should not exceed 2 years.
g. The PI should clearly define that his research proposal is a new or revised one.
h. The project's outcomes should contribute to the expected impacts listed in MOH strategy.
i. If the research proposal was previously submitted to the GDRS and rejected, it cannot be resubmitted without revision based on the technical or financial comments provided to the researcher when the proposal was first submitted. A research proposal rejected twice by the GDRS is not eligible to be submitted again.
j. The "Scientific Integrity Rules" issued by the supervisory committee of NSTIP *(NSTIP, 2012)*, must be complied with:

http://www.kacst.edu.sa/en/about/stnp/Pages/forms.aspx

k. The "Bioethics regulations" must be respected when handling living creatures or parts thereof or their genetic materials according to regulations of the National Committee of Bioethics *(NCBE, 2013)*:

http://www.kacst.edu.sa/ar/depts/bioethics/1/Regul/Bioethic.Rgl.fin.bks.pdf

l. RP should be prepared in English language but the title, name of the PI and summary should be written in both Arabic and English languages.
m. RP must be typed in Microsoft Word using font size 14 "Times New Roman".
n. All RP pages must have 2 cm margins at the top, bottom, and on each side. Line spacing must be 1.5.
o. For any technical difficulties facing a researcher during the electronic submission procedures, please communicate with the GDRS as follow:

Email: research@moh.gov.sa

Phone: +966114735038

Fax: +966114735039

2.2.2: Additive Instructions for Funded Research Projects:

p. The total project's budget should not exceed 500.000 SR.
q. Ensure that the suggested project proposal falls under one of the research priority areas of the MOH.
r. Make sure that the proposed project proposal is not already supported previously.
s. The research proposal should not be previously approved for funding and then cancelled.
t. The research proposal should not be sent to another funding agent while applying for the MOH funding.
u. The research proposal should not be similar to a project previously funded by MOH or other funding agent.
v. The research proposal must include a detailed budget, showing all project requirements in terms of human and non-human resources, as well as equipment, supplies and installations, with detailed justification of each item.

w. The potential benefits of research results may help to improve public healthcare services.

x. The GDRS has the right to incorporate the similar research proposals in one research project to be funded, and nominates the related research team in cooperation with other researchers.

y. The GDRS has the right to discontinue payment of a researcher's rewards (partly or totally) in evidence of any deviation from the approved plan.

2.3: Human Resources Guidelines:

2.3.1: For All Types of Research Proposals (either funded or non-funded):

- The PI is responsible for appointing the study team members.
- The names and roles of all participants in the project must be listed.
- Non-funded research project should have, at least, one of the employees of MOH within the research team.
- The research team must be limited to the names provided in the application form.
- The research team size must be justified, as well as the role of each one.
- The specialty of each member of the research team must be directly related to the research project activities.
- A deputy head researcher must be named when submitting the project application.
- The research team is responsible for implementing the research project according to the approved guidelines.
- If the project team requires training course(s) related to the research project domain, the PI should conduct the training program through the General Directorate of Training and Scholarship in MOH.
- The PI may delegate some of his/her responsibilities to a research team member and/or the project manager after notification of the GDRS.
- In case of PM participation, he/she must be a MOH employee.

- The project manager must be PMP certified.
- The project manager should not be participated in more than two projects concurrently.

2.3.2: Additive Instructions for Funded Research Projects:

- The PI should be one of the employees of MOH.
- A researcher should not participate in more than three funded projects concurrently, taking into account that a researcher could not be a PI in more than one project.
- The PI and Co-PI should have at least a doctorate degree or its equivalent.
- The research associate should have at least a master degree or its equivalent.
- Any participant cannot perform more than one function in the same project. In case of a necessity, the compensation is determined per one function only.
- A national or international consultant may be participated in the project regarding that the number of consultants should be limited to two per research project per year.
- The consultant's compensations should be within the project's budget and should not exceed the project duration.
- The research application must include the consultant's CV and a letter stating the consultant's consent to work in the project.

2.3.3: Responsibilities of the Principal Investigator (PI):

- PI is responsible for appointing study team members.
- PI is responsible for all actions required to manage and complete the scientific, technical, financial and administrative aspects of the project.
- Ensures that procedures used are consistent with sound research design and do not unnecessarily expose subjects to risk/harm.
- Ensures that the research project is conducted according to the GCP.

- Discloses all potentially significant conflict of interest situations.
- Initiates the hiring or assignment process after seeks approval from the GDRS.
- Is required to maintain and protect the privacy and confidentiality of all personally identifiable information of all human subjects participating in research, except as required by law or released with a written permission from the GDRS.
- Ensures the integrity and safeguarding of all research data.
- PI is responsible for ensuring the unbiased selection of an adequate number of suitable subjects according to the approved protocol
- Ensures the completion, accuracy and timeliness of the technical and financial reports (periodic, annual, final, safety (in case of clinical trials) and any other requested reports).
- Retains the scientific data in accordance with the MOH guidelines on access and retention.
- The PI may maintain a list of appropriately qualified person(s) to whom the PI has delegated some study-related duties.
- Also, the PI should adhere to the following commitments:

- The principles of scientific integrity issued by the general secretariat of NSTIP *(NSTIP, 2012)*:

http://www.kacst.edu.sa/en/about/stnp/Pages/forms.aspx.

- The published NSTIP intellectual property policy *(NSTIP, 2012)*:

http://www.kacst.edu.sa/en/about/stnp/Pages/forms.aspx

- Bioethics regulations when handling living creatures *(NCBE, 2013)*:

http://www.kacst.edu.sa/ar/depts/bioethics/1/Regul/Bioethic.Rgl.fin.bks.pdf

- The PI is responsible for all the consequences of any violation of the above.

- **Additive responsibilities in case of clinical trials:**
  - The PI and the research team should be thoroughly familiar with the safety, efficacy and appropriate use of the investigational product as described in the approved protocol.
  - PI is responsible for all study medical decisions.
  - PI has to ensure that the medical care and relevant follow-up procedures are maintained as needed by the medical condition of the subject and the study.
  - PI has to ensure that adequate medical care is provided to a subject for any adverse events.
  - PI should promptly report to GDRS, EC and SFDA in the following conditions:
    - Any deviation from or change of the protocol to eliminate immediate hazards to the subjects.
    - Any change that may increase the risk to the subjects or affecting significantly the conduct of the study.
    - All adverse drug reactions that is serious or unexpected.
    - New information that may adversely affect safety of the subjects or the conduct of the study.
    - For reported deaths including terminal medical reports and autopsy report.

2.4: Research Proposal Submission Procedures:

The following steps should be applied uniformly to all submitted RP:

- The Principle Investigator (PI) should submit his/her research proposal to the GDRS through the e-portal of the MOH (www.moh.gov.sa) using the approved form and within the announced deadlines for submission.
- Research proposal submission deadlines are as follow:

  A. For funded projects: During January and August annually.

B. For non-funded research projects: Over the year.

- All researchers are requested to go through an approved checklist before submitting their research proposals, and send the completed checklist with the filled application form through the e-portal.
- A code number is recorded, by GDRS, for each research proposal and the proposal is directed to the Internal Technical Committee (ITC) of the GDRS for further procedures.

2.5: Research Proposal Approval Procedures:

2.5.1: The Internal Technical Committee (ITC):

- The ITC will look over the project proposals and review them as per guidelines/checklist to verify that the applications and paperwork are matched with the required documents according to MOH guidelines. Then it forwards its comments, if any, to the PI (within 7 working days for non-funded proposals and within 14 working days for funded projects).
- The PI should respond and resubmit his amended proposal (within 7 working days).
- The previous steps may be repeated till complete amendment of the RP.
- In case of non-cooperation of the PI within the scheduled time, his/her research proposal may be rejected
- Then, the final proposal will be forwards, by ITC, to the DG-GDRS to take one of two decisions:

  A. For non-funded research proposals:

  The research proposal should be forwards to the Ethics Committee (EC) for a comprehensive ethical review and approval accordingly.

  B. For funded research proposals:

  The research proposals are classified in categories according to the MOH priority areas, and then referred to the Scientific Committee (SC) for thorough scientific review.

2.5.2: Ethics Committee (EC):

Responsibilities:

EC responsibilities are to ensure the protection of the rights, safety and well-being of participants involved in a research including clinical trial and to provide public assurance of that protection, by, among other things, reviewing and approving / providing favorable opinion on, the research protocol, the suitability of the investigator(s), facilities, and the materials and methods to be used in obtaining and documenting informed consent of the research trial participants.

EC should review different types of research studies, including, but not limited to, the following:

- Clinical trials.
- Epidemiological research.
- Social science research.
- Research on medical records or other personal information.
- Research on stored samples.
- Health systems research.

Criteria for EC approval of research:

Approval or disapproval is based on the ethical acceptability of the research, including:

- Scientific design and conduct of the study,
- Its social value and scientific validity,
- An acceptable ratio of potential benefits to risks of harm,
- Adequate informed consent procedures (including cultural and traditions appropriateness and mechanisms to ensure voluntariness),
- Protection of research participants' privacy and confidentiality,
- Measures to ensure protection of vulnerable populations,
- Fair procedures for selection of participants, and

- Impact of research on the communities from which participants will be drawn, both during the research and after it is complete.

Approval term:

- Approval cannot be extended beyond the approved term of study (maximum one year), unless the study has passed periodic review.
- EC rules and regulations do not permit enrolling new individuals or conducting study beyond the committee-approved period. Unless a final approval from the EC to complete the study has been obtained prior to project's expiration date, it will be automatically suspended.

Factors that affect the time frame necessary for review:

- The completeness of the initial submission.
- Review category, e.g., exempt status versus full committee review.
- Number of protocols currently under active review by the EC.
- Response time by investigators to provide requested information or amendments.

  The EC will provide PI with a written decision indicating that the EC has approved the research, requires modifications to secure approval, or has disapproved it.
- If the EC has approved the research: EC approval is usually good for a limited period of time which is noted in the approval letter.
- If the EC requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the EC. If all requested modifications are made, the EC will issue a final approval.
- Research cannot commence until this final approval is received. If PI does not accept the modifications, PI writes up his response and submits it to the EC.

- If the EC defers the research: The EC will provide a statement of the reasons for deferral and reschedule the research for review at the next meeting.
- If the EC disapproves the research: The EC will provide a statement of the reasons for disapproval and give PI an opportunity to respond in writing.

Documents required for reviewing:

All documents required for a thorough and complete review of the proposed research project should be submitted by the applicant, in the EC's working language. As applicable, this may include, but is not limited to:

1. Signed and dated EC application form, including signatures of PI (and research associates).
2. The protocol for the proposed research project, clearly identified and dated, together with supporting documents and annexes.
3. A description (which may be included in the protocol) of the ethical considerations involved in the proposed research.
4. An adequate summary of all safety, pharmacological, pharmaceutical, and toxicological data available on the study product, together with a summary of clinical experience with the study product to date (e.g. recent investigator's brochure, published data, a summary of the product's characteristics).
6. Current curricula vitae for all study team.
7. NIH certification for all study team is mandatory and required by EC.
   Free on-line NIH Course "Protecting Human Research Participants":
   This is the link to: http://phrp.nihtraining.com/users/register.php
8. All data collection forms to be used in the research project.
9. All forms, documents, advertisements to be used in recruitment of potential participants.

10. Informed consent form(s) (with date and version number) in languages understood and at a reading level appropriate for the potential research participants and when required, in other languages including:
    a. A description of measures that will be taken to ensure the protection of participants' privacy and the confidentiality of data.
    b. A statement describing any remuneration or other goods or services to be provided to study participants, including reimbursement of expenses and access to medical care.
    c. A description of arrangements for insurance coverage for research participants, if applicable.
11. A statement that the researcher(s) agree to comply with ethical principles set out in relevant guidelines.

How does PI document the informed consent?

The following are the requirements for consent documents:

- The subject or representative signs and dates the consent document.
- The individual obtaining consent signs and dates the consent document.
- Whenever required by the IRB the subject's or representative signature is to be witnessed by an individual who signs and dates the consent document.
- For subjects or read who cannot read and whenever required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the subject.

Risks on subject had been reduced to the possible minimum level by:

1. The use of known scientific procedures or methods for research design which do not expose research subjects to risks.
2. The use of appropriate and known procedures for therapeutic or diagnostic purposes.

3. Evaluation of benefits and risks that might ensue from the project.
4. Ensure that selecting research subjects has been evaluated through understanding of research objectives, place, time and method of conducting. The Committee must pay special attention in case of participation of individuals who need additional protection such as children, prisoners, pregnant women, incapacitated individuals.
5. Ensure that informed consent of the subject or his/her legal guardian had been obtained prior to actual participation in the project.
6. Ensure that informed consent has been documented.
7. Ensure that research plan includes periodic monitoring of results to maintain subject's safety and well-being.
8. Ensure that privacy of subject is preserved and confidentiality of his/her personal information is maintained.
9. Ensure that project is consistent with legislative provisions and in-Kingdom observed rules and regulations.
10. Ensure that research plan includes additional measures to protect subject's interest and rights, especially if their consent for participation could have been given as a result of pressure, compulsion or excessive attraction.
11. EC may oblige investigator to present to the subject a written extract of the study and its procedures and expected results.

Procedures for Prompt Evaluation:

EC can conduct prompt evaluation for researches which fully meet the following conditions:

1. Research projects, which are determined by the reviewer(s), those subjects of such studies are not exposed to more than the minimum range risk.
2. Research projects which do not reveal personal identity of the subject.
3. Clinical studies conducted on drugs or medical equipment when any of the following conditions is met:

a. If use of drug, as reflected in its registration information, does not have increased risks on the subject.
b. If the equipment in use is already registered and has been already utilized accordingly.
4. If biological specimens needed to achieve research objectives are not taken by invasive methods.
5. If information is obtained through non-invasive means which is normally used in the medical practice.

EC shall not approve prompt evaluation of the following:

a. Addition of new medication.
b. Addition of new equipment.
c. Addition of invasive of interventional procedure.
d. Increase or decrease of medication dose which may lead to increased risks.
e. Addition of volunteers as a demographic study.
f. Extending time period for participating subjects for other purpose than observation.
g. Change criteria of inclusion / exclusion which may involve a higher risk segment.
h. If new potential hazards are identified.
i. Collection of additional blood specimens exceeding the limit indicated in the prompt group.

Research studies which can be exempted from EC review:

a. Research involving study of data and information (currently existing) on documents, files, pathological or diagnostic specimens if such resources are generally and publicly available, or if recorded in a manner that does not directly or indirectly reveal identity of the concerned individuals through specific definitive aspects associated with those individuals.

b. Research studies which involve educational tests (cognitive, diagnostic, susceptibility or achievement) or surveying procedures, interviews or public conduct monitoring.

PI obligations after ethical approval:

Do not start research activities until having the final EC approval letter.

If it is a clinical trial:

- Saudi Food and Drug Authority (SFDA) approval:

  Research proposal for clinical trial should be referred to the SFDA for evaluation and approval. Do not start research activities until having SFDA approval.
- Do not start research activities until having the approval of departments prior to commencing research that involves their resources.
- Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
- Ensure that research staff is qualified to perform procedures assigned to them during the study.
- Personal conducts or supervises the research:

  a) Conduct the research in accordance with the relevant current protocol as approved by the EC.

  b) When required by the EC ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the EC.

  c) Do not modify the research without prior EC review and approval unless necessary to eliminate apparent immediate hazards to subjects.

  d) Protect the rights, safety, and welfare of subjects involved in the research.

Controls of sending genetic materials for research Purposes outside KSA:

According to the regulation of the National Committee of Bioethics (NCBE),

When it becomes necessary to send biological specimens or participation in a research study conducted outside Saudi Arabia, the following must be observed *(NCBE, 2013)*:

1. The PI should be verifying that such study cannot be conducted in the Kingdom.
2. Research study should be conducted with a world-renowned research institution that has well-known experience in the field of research.
3. The PI should have a written consent of the local Ethics committee to send samples abroad, by sending an official letter explaining the causes of transmission, the quantity and the type of samples, to whom it will be sent and to notify the NCBE for approval.
4. An agreement must be made which should secure the rights of the Saudi patient and investigator as well as the national rights. It must be presented in the form of participation in a research study which must be approved by a local committee of bioethics at the reporting institution of the investigator who is interested in sending patient specimens to institutions outside Saudi Arabia for research purposes.
5. Ensure that the research study has not been previously conducted or registered in the Kingdom, to avoid duplication of research activities.
6. If it appears that another Saudi investigator or institution conducts the same study with the support of Saudi institutions or hospitals, no biological specimens should be sent outside the Kingdom. Cooperation must be made with the progressing research inside the Kingdom, ensuring that research terms, conditions and ethics are guaranteed for participating patients.
7. Biological specimens must carry numbers and codes only with no personal information of the patient from whom specimen is taken.
8. NCBE must be notified in writing of the contents and the parties conducting the research study to verify that such study cannot be conducted in the Kingdom neither is there another research dealing with the same

subject. The committee will also ensure that international institutions and/or investigators cooperating with the study are known for that type of research. Moreover, it will review the national rights and determine the extent of benefit; the in-Kingdom medical institution can gain from the results of such research. The NCBE may reject the initiation or completion of the study if it appears to the committee that it is of no benefit for the Saudi community, or if it is directly or indirectly proven to be detrimental to the community. This right of the committee must be clearly defined in the agreement concluded between the PI and the overseas institution.

Follow-up reviewing and monitoring of research proposal:

The procedure for follow-up review takes the following into consideration:

- Documents to be reviewed, including but not limited to:
  1. Progress reports, final report.
  2. Audit reports, independent of the researcher and the sponsor (e.g. institutional internal audits)
  4. Experiences of the participants and potential participants (e.g. independent observation of the informed consent discussion, independent surveys of participants experiences).
  5. Notification from the applicant with regard to suspension / premature termination or completion of the study.
- The intervals for follow-up reviews, which should be determined by the nature of the research project but should generally be at least once a year.
- Circumstances that will trigger follow-up reviews, in addition to those that are regularly scheduled, including the following:
  1. Any protocol amendment likely to affect the rights, safety, and/or well-being of the research participants or the conduct of the study.
  2. Serious unexpected adverse events related to the conduct of the study or study product.

3. Any event or new information that might affect the potential benefits or risks of harm involved in the study.

2.5.3: The Scientific Committee (SC):

- The SC reviews and ranks the research proposals that referred by GDRS for funding, based on the procedures and guidelines established by the commission and in a manner that gives due consideration to the scientific integrity of the research proposals.
- After evaluation, the SC notifies the GDRS of its decisions on the research projects through an evaluation summary report for each proposal. Most recommendations are along the following lines:
  - To unconditionally accept the proposal,
  - To reject it, but encourage revision and invite resubmission,
  - To reject it outright.
- The funded research project should not be implemented without a written approval of SC.
- The chairman of the SC reports to the Research Priorities Adoption Committee (RPAC) a list of the recommended research projects for funding sorted according to the scientific merit and available fund, to take the final decision for funding.

2.5.4: The Research Priorities Adoption Committee (RPAC):

- The RPAC is a higher committee to study the research proposals that have been approved by SC, checks whether the proposal is in scope and then ranks the proposals according to the following criteria:
  1. Impact on health.
  2. Applicability and relevance to KSA.
  3. Contribution to expected impacts listed in MOH strategy.
  4. Urgency for decision making.
  5. Community demand.

6. Available budgeting.
7. Political and ethical acceptability.
8. Appropriate allocation and justification of the resources.
9. Avoidance of duplication with other current and future projects.
10. Economic impact and cost-effective ratio.

- The Research Priorities Adoption Committee makes the necessary decisions accordingly and enrolls the approved research project for funding with their allocated budgets based on the final ranking list and the available budget.
- Then, the RPAC notifies the GDRS with the final research project's list approved for financial support.
- The chairman of the RPAC recommends to the Minister of Health for approval of the funded research plan.

2.5.5: Additive instructions for conducting clinical trials:

- A Clinical Trial Authorization (CTA) is required for any clinical trial to be conducted in KSA. The application for a CTA is made to Saudi Food and Drug Authority (SFDA) who is responsible for advising on the regulations and the requirements for CTA.
- All clinical trials must be registered at the SFDA according to the clinical trials Memo No. 3476 on the date of 13/1/1431 H.
- The PI for any clinical trial must be Saudi.
- There are two classes of study drugs are initially permissible to be included in clinical trials within MOH facilities:
  1- Approved drug undergoing clinical trial for new indications, methods of administration, dosage, etc.
  2- Approved drug granted for marketing, used in clinical trial as a study drug, comparator drug or concomitant drug for approved indicators, approved method of administration and dosage.

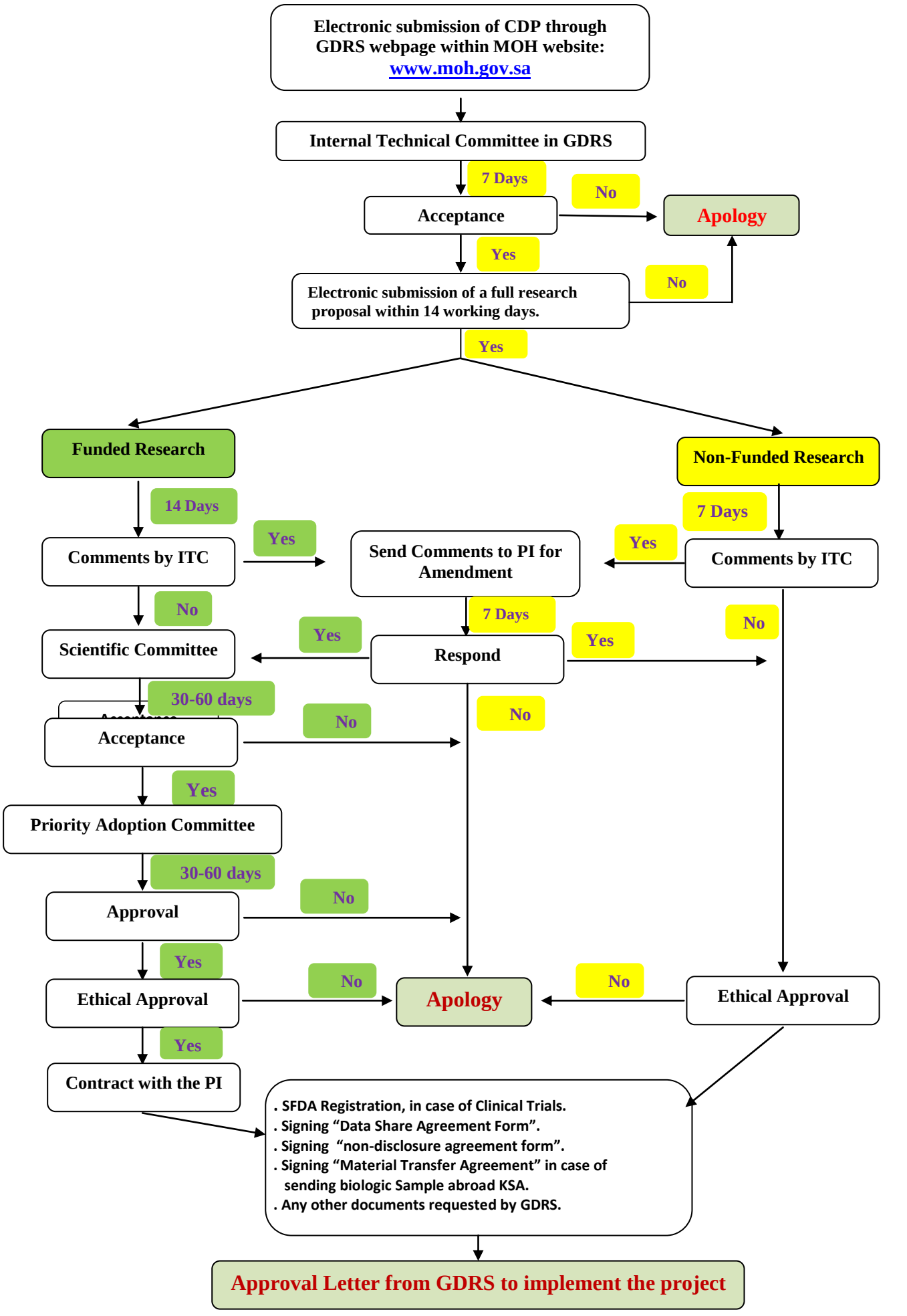
- In addition to submitting all health researches according to "MOH guidance manual", clinical trials should be conducted on the basis of the regulations available from the SFDA on clinical trials (SFDA, 2013):

  http://www.sfda.gov.sa

- Approval of the trial by EC of each local trial institution is required to initiate a study and must be enclosed for research involving human subjects as also animal experiments.
- In human beings, for the use of different ionizing radiation for diagnosis and treatment (x-ray, gamma ray, proton, beta particles, etc.), radiation limits for the use of such materials should be accordance with the limits set forth by the regulatory authority for such materials.
- Investigator's Brochure (IB) for the investigational product(s) should be included according to the approved drug submission application form.
- Approval letter from the SFDA is required in the following cases:
  - Change in dosage regimen or treatment options.
  - Off label indication.
  - Using drugs for unregistered indication.
- Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the GDRS according to the reporting requirements and within the specified time periods.
- It is essential to inform the GDRS, EC and SFDA about all expected and unexpected (not serious) adverse events for drugs in the trial within 15 days. In case of serious adverse events that may lead to (death, life threatening, hospitalization, disability or birth defect), the notification should be immediately within 7 days.
- For SFDA guidelines and practical directions to submit and register your clinical research, please, go through the SFDA website:

  (www.sfda.gov.sa).

The following is schedule for the process to manage research proposals within MOH:



2.6: Financial Regulations:

2.6.1: General Financial Guidelines:

With the exception of conclude contracts or invitations between MOH and research experts, universities, research centers or consulting offices, the financial aspects of the funded projects will be determined as follows:

- The total project's budget should not exceed 500.000 SR.
- A detailed budget over the implementation period should be included in the proposal using the approved form, with justification of each item.
- The project duration and the kick off date should be specified.
- After signing a research project contract, the first and subsequent fund installments will be released in phases to PI in accordance with both the "Financial Regulations of Ministry of Health" (Item 238) and the MOH bylaw for research No. 40464 and dated 3/9/1433 H *(MOH Bylaw, 2012).*
- It is advisable that the PI should not make any financial or personal commitments in the absence of an approval letter from the GDRS to start project’s implementation, if does so, he/she will be at his own risk.
- The allocated fund should be expended in accordance with items mentioned in the budget section of the approved proposal.
- The day on which the first installment of the fund is received by the PI will be considered as the starting date of the research project.
- Researchers are informed that, agreed budget for the research will not be changed and no request for increasing it will be deemed at any stage of research conduction.
- It is not permissible to increase the project budget or make any redistribution in items except after receiving a written approval from GDRS.
- No payments should be activated before the project kick off and after closure of the project.

2.6.2: Financial Guidelines for Human Resources:

- The total payments received by any research team member should not exceed the equivalent of compensation for three projects per month (Provided that he/she is a PI for only one project in the same period).
- A research team member should not receive two compensations at the same time for the same research project.
- The total budget for all the team members in the research project must not exceed 50% of the total budget of the research. The research projects that depend mainly on man power may be excluded from this rule after approval of the GDRS.
- Compensation for the project staff is made based on the progress achieved and the roles and responsibilities of each member.
- Any payment to the research team should not be permitted except after approval of the technical and financial reports of that period of time and after fulfillment of the financial settlements of the previous period.
- The reward of the consultant should be approved only after submitting a report by the PI on the task achieved in the consulting period. Also, this report should be associated with a comprehensive report by the consultant.
- If the required consultation was achieved from the consultant in his office inside/ outside the Kingdom with no need to attend to the implementation site, he/she shall receive the reward as an internal (from inside the city) consultant.
- The number of consultants, either internal or external, should not exceed two / year.

2.6.3: Field Trips:

The research team may activate an internal or external research trips to collect scientific data related to the research field, according to the research plan taking into account the following instructions:

(1) The request should be submitted to GDRS at least 30 days before date of trip using the approved form and taking into account the maximum funding level for field trips.

(2) The budget for the field trips must not exceed 50.000 SR / the duration of the projects.

(3) The Internal Trips:

- The trip should be necessary to achieve the tasks and objectives of the research.
- The total number of days of all field trips should not exceed thirty days per person per year after a written approval of the researcher's employer, and according to the Civil Service System.
- The researcher should provide a summarized report about his trip after his return.

(4) The External trips:

- The trip should be necessary to achieve the tasks and objectives of the research.
- The trip should be approved in the research plan.
- The researcher should provide a full program for the trip's activities and how this trip is important for research achievement.
- Identify the duration of the trip.
- Approval document from the site to be visited.
- A written approval of the researcher’s employer, and according to the Civil Service System.

(5) The researcher should provide a summarized report about his trip after his return.

(6) Travel and miscellaneous expenses: if travel and miscellaneous expenses exceed 10% of the budget, PI need to take approval from the GDRS after providing details of this item.

2.6.4: Conferences and Seminars:

The research team may attend specialized scientific conferences or seminars, according to the research plan taking into account the following instructions:

(1) The conferences could be attended during the second year taking into account the maximum funding level for conferences.

(2) The request should be submitted to GDRS at least 60 days before date of the conference using the approved form.

(3) The expenses of conferences must not exceed 50.000 SR including tickets.

(4) The participation of a conference should be through an accepted paper derived from the research (paper, poster), subject to the provisions of intellectual property right (Article 4.6).

(5) The participant should provide a report and the certificate of attendance within 30 days after his/her return.

2.6.5: Printing and Publication:

The printing and publication costs should not exceed 5% of the total budget in the whole project's period.

2.6.6: Dispensing Aspects:

The dispensing aspects that covered by the research budget:

1. The compensations of the research team and participants.
2- The compensations of the reviewers and consultants.
3- Costs of equipment, materials and soft wares.
4- The compensations of the committees presidents and members.
5- Costs of printing and publishing.
6- Field trips and scientific conferences.

The following template summarizes the compensation of each dispensing item according to MOH bylaw for research and studies *(MOH Bylaw, 2012)*:

Research Participant's Compensation Template

Job Title	Compensation	Instructions	Notes
Principle Investigator	5000 SR/month	The participation of a researcher should not exceed one research as a PI and two researches as a research associate, during the same period.	
Research Associate	3000 SR/month		
Research Assistant	100 SR/hour	No more than 4 hours daily, for a maximum of 3000 SR / month.	
Field Auditor	100 SR/hour	No more than 4 hours daily, for a maximum of 3000 SR / month.	
Committee President	700 SR / Setting	For a maximum of 21000 SR / year.	
Committee Members	700 SR / Setting	For a maximum of 21000 SR / year.	For each member.
Project's Reviewer	2000 SR / Proposal		
Internal Consultant from inside the city	500 SR / Day	For a maximum of 10000 SR / year	The number of consultants, either internal or external, should not exceed two / year.
Internal Consultant from outside the city	1000 SR / Day + Flight tickets	- For a maximum of 14000 SR / year including the costs of accommodation and subsistence. - For a maximum of two visits / year.	
External Consultant	2000 SR / Day + Flight tickets	- For a maximum of 20000 SR / year including the costs of accommodation and subsistence. - For a maximum of one visit / year for each consultant.	

Instructions for Non-Human Resources Funding Items

Internal field trips	Maximum 50.000 SR / duration of project for all project's trips.	- The trip should be necessary. - The maximum period of the field trips for each person should not exceed (30) days per year.
External field trips		- The trip should be necessary. - The trip should be approved in the research plan. - The researcher should provide a full program for the trip's activities. - Identify the duration of the trip. - Approval of the site to be visited. - Approval of the employer.
Conferences and Seminars	Maximum 50.000 SR During the 2nd year of the project.	- The conferences could be attended during the second year. - The participation of a conference should be through an accepted paper derived from the research (paper, poster). - The participant should provide a report and certificate of attendance within 30 days after his return.
Printing and Publication	should not exceed 5% of total budget in the whole project's period.	
Training		Through the General Directorate of Training and Scholarship.

2.6.7: Dispensing Mechanism:

Unless the contract provides otherwise, the approved fund for the research should be discharged from the MOH financial item for research and studies (Item 238), within the approved total budget of the project, in the following manner :

- 20% of the total funding: should be discharged as a request an advance within fifteen days after signing the contract.
- 60% of the total funding: should be discharged as a request an advance, on steps, after submission and approval of the progress technical and financial reports for each step and after fulfillment of the financial settlements for the previous period.
- 20% of the total funding: should be discharged as a request an advance, after submission and approval of the final technical and financial reports by the SC and after fulfillment of the financial settlements for the previous period.
- Equipment, supplies and other needs should be purchased according to MOH regulations and guidelines.

2-6-8: Payment Authority:

- Less than 50,000 SAR: Principal Investigator or Project Manager.
- 50.000 -250.000 SAR: Director of Research Grants Office in GDRS.
- 250.000-500.000 SAR: Director General of the GDRS.
- More than 500,000 SAR: The Higher Authority.
- Any other financial instructions that may be issued by the MOH.

2.6.9: The Sources of Funding:

- The MOH financial item for research and study in MOH (Item 238).
- All research items in the self-employment programs of MOH .
- Further monetary consolidation approved by the higher authority.

2.6.10: Recruitment Process:

Human resources can be recruited on a research project provided the following instructions:

- Recruitment applications for the project should be submitted via the PI to the GDRS.
- The recruitment compensations should be within the project's budget and should not exceed the project duration.
- The contract between the PI and the engaged person must be signed indicating the first day of work. GDRS must have a copy of the contract.
- The contracting party and the PI should sign a contract using the approved project services contract form.

2.7: Factors that may Cause Rejection of a Research Project from Funding:

- If the research proposal is not submitted through the GDRS-MOH e-portal.
- If the submitted research proposal is not aligned with one of the MOH health research priorities.
- If the research proposal is not entirely submitted according to the MOH research submission manual.
- If the research proposal was previously submitted to the GDRS and rejected, it cannot be resubmitted without amendment based on the comments provided to the PI when the proposal was first submitted. If the research proposal rejected twice, it is not eligible to be submitted again.
- If the submitted project is similar to another project previously funded by MOH or other funding agent.
- If the research proposal was previously approved by MOH for funding and then cancelled.
- If the research proposal has been sent to another funding agent while applying for MOH funding.
- If the research entirely or partly plagiarized from another research.

- If the research proposal is not approved by SC, RPAC, EC or SFDA (in case of clinical trial).
- Noncooperation of the research team with remarks and comments of the GDRS team during implementation of the research project.
- Evidence of belongings or comments on the PI or one of the research team involved in previous MOH research.
- If the project is not started at the approved kick off time, without approval from the GDRS.

2.8: Forbidden Actions for PI without a Prior Written Approval from GDRS:

- Delay of the Project's kick off.
- Change, addition or exclusion of any research team member.
- Any change or modification for the approved work-plan.
- Any change or modification for the approved budget.
- Activation of the contracts with individuals or other entities.
- Initiate any modifications to the approved goals or methodology of the project.
- Make any modification or redistribution in the approved funding items.
- Initiate any publication of a scientific paper, patent or product.
- Addition of author(s) outside the research team or acknowledge any other entities to the published scientific papers or patents.
- Initiate hiring or assignment process.
- Delay of submitting the financial and/or technical report beyond the scheduled time.
- Temporal halt of the project.
- Extension of the project beyond the approved protocol.
- Disseminate information on research or research output (publication, patent, product or others).
- Nomination of the research to national, regional or international awards.

3- Guidelines for Research Proposal Implementation:

3.1: General Guidelines:

After complete fulfillment of all steps that previously described in research proposal submission guidelines (Articles 2.1 to 2.8), the following instructions should be considered:

3.1.1: How to Get an Approval Letter to Implement Your Research Project?

3.1.1.1: For all Research Projects:

- The following documents should be completed by the PI before acquiring an approval letter to implement the research project in a MOH's facility:
  - A written approval letter from the ethics committee.
  - Registration in the SFDA in case of clinical trials.
  - Fulfillment of the "Data Share Agreement Form".
  - Fulfillment of the "Material Transfer Agreement" in case of sending a biologic sample for analysis outside KSA.
  - Nomination of a deputy head researcher, associated with his CV.
  - The research team should sign the "Undertaking of the project team" using the approved form.
  - PI consent that he/she has read the MOH research submission manual thoroughly.
  - PI consent of the delegated responsibilities, if any.
- After complete fulfillment of those documents, the DG-GDRS, will sign an approval letter and submit it to all MOH facilities where the research project will be conducted. Also, a copy of the approval letter should be sent to the PI for notification.

3.1.1.2: For Funded Research Projects:

- In addition to the establishment of all the documents previously described (Article 3.1.1.1), the following documents should be fulfilled:
  - Two signed copies of the project's contract form, between DG-GDRS (1st party) and the PI of the project (2nd party) once funds are available to start implementation.
  - A copy of the approved work plan, including the date of kick off the project (it should be within 60 days of the date the PI signs the contract).
- After complete fulfillment of these documents, the DG-GDRS will sign an approval letter and submit it to all MOH facilities where the research project will be conducted. Also, a copy of the approval letter will be sent to the PI for notification.

3.2: Other Regulating Rules:

3.2.1: Withdrawal of the PI:

If the PI wishes to withdraw from the project before its completion or if he/she wishes to give up his/her responsibilities as a head researcher, the following steps should be considered:

- The PI should submit the approved official form to the GDRS discussing, in details, the reasons for his/her decision for withdrawal from the project.
- The following documents should be included:
  1. Nomination of a replacement PI associated with his/her CV and his/her consent to complete the project and take all the responsibilities of PI.
  2. The nominated PI should have all qualifications that were previously described in the "GLOSSARY".
  3. A technical and financial report on the elapsed project period.

4. An official clearance from any financial or other belongings related to the project and he/she should return the balance of unused/uncommitted funds to MOH.

- If the PI is a single researcher and shows inability to complete the research, he/she should return the balance of unused funds to MOH.
- If none of the researchers wishes to take on the position of the PI, the GDRS can nominate a new PI.
- All the responsibilities of the PI will be shifted automatically to the deputy principal investigator if the PI quits from research project for reasons beyond his/her capacity or until the assignment of a new head researcher.
- At the end of the project, it should be noted for that change according to the time and tasks for each one in the project.
- It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.2: Transfer the PI from the Implementation Site:

In case the PI transfer away from the implementation site, either before or after the beginning of project implementation the following procedures should be considered:

3.2.2.1: Research Projects with a Single Researcher:

(a) If the transition before the start of the project, the PI should provide the GDRS with a written agreement of the new site to conduct the research project, then to modify all documents (administrative, contracts, budgets,....) to become within the name of the new party.

(b) If the transition during implementation of the project, all the documents and financial transactions remain in the possession of

the original party, unless it expressed unwillingness to do it, in this case we must apply the previously mentioned paragraph "A" (Article 3.2.2.1).

3.2.2.2: Research Projects with Many Researchers:

(a) The research team should nominate one of its members as a head researcher regarding that he/she should have all qualifications that were previously described in the "GLOSSARY".

(b) The original PI may be continuing in the research as a consultant or as a research associate, after approval of the new PI and GDRS.

(c) The name of the original PI may remain linked to the research as follow:

- Principal investigator: If he/she terminates of at least 75% of the tasks and burdens of research assigned to him.
- Research associate: If he/she terminates from 50 - 74% of the tasks and burdens of research assigned to him/her.

(d) It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.3: Withdrawal or Replacement of a Member of the Research Team:

In case of withdraw or replacement of a research team member from the project, the following procedures should be considered:

- For replacement of a research team member: The PI should notify the GDRS using the approved official form, explaining the reason(s) of that decision associated with the CV and approval letter from the replacement person.

- It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.4: Delay of the Project's Kick off:

The PI may request to delay the starting time of the project implementation. The following procedures should be considered:

- The request to delay the project starting time must be submitted by the PI using the official forms and explaining the reasons for the request to the GDRS.
- The delay must be once only and it should not exceed 60 days.
- The GDRS reviews the request and formally informs the PI of its decision.
- The financial dispensing is prohibited during the lag period.
- If the project does not start at the new kick off time, the project may be cancelled either funded or non-funded project.
- It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.5: Temporal Halt of the Project:

The PI may request to temporary halt the project implementation. The following procedures should be considered:

- The request to halt the project should be submitted by the PI using the official form and explaining the reasons for the request to the GDRS.
- The temporal halt of the project must be once only and it should not exceed 90 days.
- The GDRS reviews the request and formally informs the PI of its decision.
- The financial dispensing is prohibited during the halting period, except for mandatory commitments and after permission from GDRS.

- The halting period should not be calculated from the approved project's period.
- Accordingly, the GDRS should re-define new set times to provide the technical and financial reports.
- It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.6: Project Suspension or Cancellation:

The GDRS may suspend or cancel the research project for any of the following reasons:

- Delay to kick-off the project's implementation without a written consent from GDRS.
- Noncooperation of the PI/PM in responding to comments or questions of the GDRS in due time.
- The addition or change of research team members without a prior written approval from the GDRS.
- Major deviation from the approved project protocol.
- Serious deviation from the principles of GCP.
- Delay for the submission of the technical and/or the financial reports to the GDRS on the scheduled deadlines.
- Monitoring of evidences for serious technical, administrative and/or financial shortcomings during implementation of the project.
- Violation or transposition of any budget item without a prior written approval of the GDRS.
- Noncompliance with the "Scientific Integrity Rules" published by the supervisory committee of the NSTIP *(NSTIP, 2012)*:

http://www.kacst.edu.sa/en/about/stnp/Pages/forms.aspx

- Noncompliance with the "Bioethics Regulations" when handling living creatures or parts thereof or their genetic material *(NCBE, 2013)*:
http://www.kacst.edu.sa/ar/depts/bioethics/1/Regul/Bioethic.Rgl.fin.bks.pdf
- Noncompliance with the "intellectual property Policy" published by the supervisory committee of the NSTIP *(NSTIP, 2012)*:
http://www.kacst.edu.sa/en/about/stnp/Pages/forms.aspx
- Withdrawal of the PI, with failure to attain a replacement PI.
- Serious conflict among the research team members that may affect the quality of the project's implementation.
- A penalty may registered by the DGRS to a research team member who is proved to be involved in the project suspension or cancellation according to GDRS instructions (Article 4.8.3).
- It is the responsibility of GDRS to take appropriate decision and follow up these procedures according to the administrative and financial regulations.

3.2.7: Project Extension:

- If a project extension time is needed to complete the work plan, the PI must submit a request to the GDRS explaining the reasons for the project extension, at least 60 days before the project end date using the approved form with the following documents:
  - Technical report for the last year of the project.
  - A technical plan (no more than 2 pages) for the extension period.
  - A financial report for the elapsed period, showing the remaining budget.
  - A detailed budget for the extension period, excluding rewards of the research team and participants.
- A budget supplementation cannot be requested for the extension period.
- The extension period should not exceed 6 months for once.
- The extension period should be managed according to the same regulations conducted in the original period.

4- Guidelines for Research Project's Follow-up and Outcomes:

4.1: Research Performance Progress Reports (RPPR):

- The PI should submit three types of RPPR as follow:

  - Periodic report.

  - Annual report.

  - Final report.

- Safety Reporting may be provided to inform about adverse reaction(s).
- Additive progress reports may be required to update any sequence of events, during the project's implementation, according to the request of the GDRS.
- The PI should provide RPPRs using the approved forms as follows:

4.1.1: For All Research Projects:

- The PI should submit a periodic technical report to the GDRS at the end of the first 6 months of each Hijri year, using the MOH report forms (one hard copy and a CD), within 15 days from the targeted period's deadline, discussing the technical progress achieved in the elapsed six months of each year starting from the project's kick off date.
- The PI should provide an annual technical report to the GDRS at the end of each Hijri year, starting from the project's kick off date, using the MOH report forms (two hard copies and two CDs), within 30 days from the targeted year's deadline, discussing the technical progress achieved of the year elapsed.
- The PI should provide a final technical report upon project completion using the MOH report forms (two hard copies and two CDs), within 60 days from the approved project deadline discussing the achievements and outcomes since the beginning of the project.
- Safety Reporting: In case of conducting a clinical trial, it is essential to inform the GDRS, EC and SFDA about all expected and unexpected (not serious) adverse events for drugs in the trial within 15 days, except for

those SAEs that the protocol or other document (e.g., Investigational product brochure) identifies as not needing immediate reporting. In case of serious adverse events that may lead to (death, life threatening, hospitalization, disability or birth defect), the notification should be immediately within 7 days.

- The GDRS has the right to request additional report(s) from the PI when indicated.
- All technical reports should be reviewed by the ITC and the comments will be forwarded to the PI who should follow such comments.
- The PI should respond to the comments and feedbacks of the GDRS within 30 days from date of receiving notes.
- If the PI did not commit to amend the required comments and modifications and resubmit the upgraded report to the GDRS within 30 days from date of receiving notes without a written approval from the GDRS, the GDRS has the right to apply a penalty according to GDRS instructions (Article 4.8.3).

4.1.2: Additive Instructions for Funded Research Projects:

- The PI should submit financial reports, in addition to the above-mentioned technical reports (Article 4.1.1) and at the same dates and the same requirements.
- All reports should be reviewed by the ITC and the comments will be forwarded to the PI who should follow such comments.
- Also, The SC should evaluate the annual and final reports of the projects (technical and financial), then notifies the GDRS and the RPAC of its decisions.
- The PI should respond to the comments and feedbacks by the GDRS /SC's within 30 days from date of receiving notes.
- GDRS may request additional reports from the PI when indicated.

4.2: Delay in the Submission of Project's Reports:

- The PI may delay submission of a financial or technical report beyond the stipulated deadlines after a written approval of GDRS regarding the following conditions.
  - The request to delay a report's submission should be reasonably justified.
  - The request of delay should be submitted at least 30 days before the original deadline.
  - The new deadline is not more than 30 days from the original deadline for all types of reports.
- It is the responsibility of the GDRS to take the appropriate decision and follow up these procedures according to the administrative and financial regulations.

4.3: Internal Auditing:

- The field auditor performs financial, operational and system audit in a manner that reflects the highest professional standards that complies with the MOH guidelines.
- The field auditor will then provide prompt and accurate reporting of audit results to the DG-GDRS.
- The tasks of the internal audit are the following:
  - Provide a continuing, comprehensive risk-based review of the operational and financial processes.
  - Provide independent support for the effective internal control system.
  - Promote the establishment of best practices.
  - Maintain the research participant safety and rights.
  - Provide leadership to key decision-makers in the identification of operation, finance and control risks.
  - Monitor and evaluate risk management procedures and internal controls.
  - Support the corporate governance and public accountability process.
  - Communicate collaboratively with the research team and GDRS.

4.4: Project Closure:

- The PI and other research team should not be free of their responsibilities until the project is cleared financially and technically, all the research outputs of the project are delivered (including publications, patents, new products or others) and the PI has a writing clearance document.
- If a project extension time is needed to complete the work plan, the PI must submit a request to GDRS according to the approved process (Article 3.2.7).

4.5: Ownership of Equipment:

- The devices, equipment, materials, others that are secured or manufactured from the support provided to the research by MOH are the property of the GDRS alone, and are in the custody of the PI to be used for the duration of the implementation of the research, and he is committed to maintaining their safety and maintenance.
- GDRS should continue having the ownership of this custody for a period of two years after closure of the project, and after the end of that period become the property of the indigenous part.
- GDRS has the right, during the period of ownership, to transfer part or all custody to another research in the same or other beneficiary part, or be waived to indigenous part, or permanently withdrawn from that side.
- All custody should be delivered to the GDRS sound and usable.

4.6: Intellectual Property Rights:

1. The PI must adhere to the intellectual property policy *(NSTIP, 2012)*.
2. In case of conducting a research or study sponsored by MOH, the full research outputs will be owned to the Ministry, unless the contract provides otherwise.
3. If the project is not classified as confidential, and there is a desire to publish some or all of the research results, Intellectual Property rights (IPR) of the MOH as well as those of the participants in the research project must be respected.

4. The MOH has the right to conceal the results of a project if this is in the public interest or contains confidential information.
5. The results of any research project as publication, patent, new products or others should not be published, launched or shared with others unless a prior written permission is obtained from GDRS.
6. Any research output as publication, patent, product or others must include credits to the contributions of MOH and individuals involved with the project.
7. The support provided by MOH for the project must be recognized when the research is disseminated in scientific papers, conferences or any other publication methods.
8. Any scientific product from the research (bulletin, article, scientific paper, computer programs soft wares, or other materials related to the research) should bear the, recognition of the MOH support for the research, and the text should be as follows:

   "This article / paper / bulletin / ….. Contains studies, results, recommendations, ….. of the research titled "……" has been supported by the Ministry of Health, number……. and date / / .
9. All published material through any media outlet, with the exception of scientific articles published in scientific journals, should have the MOH logo and a formula to acquit the MOH as follows:

"All opinions and findings, conclusions and recommendations mentioned in this publication are of the author and do not necessarily reflect the view of the Ministry of Health".

10. When publishing research project results, scientific periodicals listed in the international information bases such as ISI, SCOPUS, in addition to other world databases, should be selected.
11. The PI should deliver two copies of all the projects scientific outputs such as scientific papers, patents and others, to the GDRS, after publication.

12. MOH has the right to share in the ownership of any resulting patent or product, and in case of a financial return, the income should be divided equally between MOH and research team until the supporting fund of the project is covered, unless the parties agree otherwise in the grant contract.
13. In case of the desire of research team to nominate the research to award (national, regional and international) they should obtain a prior approval from GDRS, with an emphasis on the research team to recognize the support of the ministry for research, and the acquired revenue in such a case will be divided as previously described in item 12 of article 4.6.

4.7: Confidentiality:

- PI is required to maintain and protect the privacy and confidentiality of all personally identifiable information of all human subjects participating in research, except as required by law or released with the written permission of the GDRS.
- Even if a research protocol does not call for direct contact with individual subjects, the GDRS still must determine whether or not MOH will permit access to identifiable health data. Also, there are confidentiality concerns when researchers want access to personally identifiable data from health care providers.
- Biological specimens and participant's data must carry numbers and codes only with no personal information of the patient from whom specimen is taken.
- **Data Share Agreement (DSA):**

  GDRS expects valuable data arising from the research projects to be made available to the scientific community with as few restrictions as possible so as to maximize the value of the data for research and for eventual patient and public benefit. Such data must be shared in a timely and responsible manner. One of the best ways of achieving this is to ensure that information are

properly preserved for sharing and informed use beyond the originating research teams.

- **Non-Disclosure Agreement (NDA):**

  A Non- Disclosure Agreement (NDA) is a legal agreement between GDRS and the PI, which outlines information the parties wish to share with one another for certain evaluation purposes, but wish to restrict from wider use and dissemination. The parties agree not to disclose the non-public information covered by the agreement.

- **Retention of Data:**

  PI will maintain all research records for at least five years after completion of the research. If the research is sponsored, contact the sponsor before disposing of the research records.

4.8: Responsibilities and Accountabilities:

4.8.1: Principal Investigator:

- The PI is responsible for all actions required to manage and complete the scientific, technical, financial and administrative aspects of the project.
- The rights and welfare of the participants involved in the research need to be adequately protected.
- PI should obtain a freely given informed consent from research participants.
- The PI is responsible for all the consequences of any violation during the project's implementation.
- All ethical violations should be reported immediately to EC for reviewing such violations and make the appropriate decisions to be forwarded to PI.
- In the event of injuries to the research participants, MOH will not be responsible with regard to administrative, legal and financial issues arising

from such injuries. Rather PI will be accountable for such safety issues while carrying out the research.

- In case of injury to the research assistants or other research workers, MOH will not be responsible with regard to legal and financial issues arising from such injuries. Rather PI will be accountable for such safety issues while carrying out the research.
- PI should place safeguards against occurrences of any injury both to the research participants and assistants while conducting research.
- PI should help to arrange treatment of research participants in case if such injuries occurring to them during conduction of research project.
- In case of termination of research due to any reasons, PI should immediately inform EC.
- In case of any new information affecting the benefit/risk ratio of approved proposal, PI should immediately inform EC for taking possible action.
- In case of PI shows inability to complete the research, he/she should nominates a substitute and notify the GDRS through the approved form before his/her withdrawal from the research project as described previously (Article 3.2.1).
- If the PI shows inability to complete the research, he/she should return immediately the balance of unused funds to MOH and he/she should nominate a replacement PI before his/her withdrawal from the project.

4.8.2: Researcher's Team:

- No researcher is allowed to use MOH facilities such as laboratory kits, human resources, others while conducting research at MOH settings except after getting approval from the head of the institution.
- Researchers are informed that data should be stored securely and only persons authorized by PI are permitted to access to the database.

- Researchers are informed that data collected must be used only for the approved proposal.
- Personal identification data should only be collected when necessary for approved proposal.
- Researchers are informed that personal identification data should be anonymized before data analysis (or transfer to other site for the same purpose) and secondary disclosures of personal data are not allowed.
- It is prohibited to conduct any research at MOH setting without the prior permission from GDRS.
- Publication (by any means) is prohibited without the prior permission from (GDRS) and should include the rules of MOH in the research.

4.8.3: Ministry of Health:

- GDRS is accountable for ensuring that MOH research projects planned, designed, conducted, coordinated, accessible, of high quality efficient and effective.
- In case a project requires experimenting on living creatures or on the environment, MOH is not legally or financially liable for any accident, or any health injuries, or human loss, or any compensation for damage caused due to any research conducted in its facilities. The PI must obtain the necessary licenses and permissions from the relevant authorities, in advance, to conduct any experiment with possible negative effects of humans, animals or the environment.
- MOH will not mediate in any court complaint(s) against PI filed by research participants and assistants.
- MOH will not pay any sort of compensation for any financial or other court penalty accrued to the PI during or after research completion.
- A penalty may be registered in case of any violation for the commitment of this manual, in the form of :
  - Discounting a part or all of the PI and/or research team compensation.

- The GDRS has the right to assign another PI and/or a new research team, to finish the project.
- Cancellation of the project and the GDRS may decide to cease funding of the project.
- The GDRS has the right to prevent the PI/ a research team member from participation in any MOH research project for one to three years depending on the GDRS's decision.

- The PI and the research team are in such case fully responsible for the consequences, including refunding payments disbursed to research team.

4.9: Moral Obligation:

Any health research must be conducting in accordance with the "principles of ethics of research on living creatures" issued by Royal Decree No. (M / 59) dated 14 / 9 / 1431H.

4.10: Legal Issues:

- In matters where there is no specific related article in these regulations, MOH effective rules or decisions should be followed.
- In case of failure of the GDRS and the legal administration to resolve any dispute, the affected party may resorted to the laws and applicable regulations of the Kingdom of Saudi Arabia.
- The GDRS has the sole right to interpret or amend any items in these articles after a written approval from the higher authority.

4.11: Application of the Regulations:

1. These regulations are applied to all research projects that are conducted in MOH's facilities.
2. This guiding manual is effective from the date of its adoption.
3. This manual may be updated every five years from the date it is issued or as needed according to the view of the GDRS / Higher Authority.

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