Research Ethics and Regulatory Requirements
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Section 1. Human Subjects Research

The Supreme Council of Health (SCH) regulations for the protection of human subjects, Policies, Rules and Regulations for Research Involving Human Subjects (SCH Regulations), provide a framework, based on established, internationally recognized ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by Qatar National Research Fund (QNRF).

The SCH Regulations stipulate that the awardee organization(s), whether domestic or foreign, bears ultimate responsibility for safeguarding the rights and welfare of human subjects in QNRF supported activities. SCH defines research as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to general knowledge. Activities which meet this definition constitute research for purposes of this document, whether or not they are conducted or supported under a program which is considered research for other purposes. Human subject means a living individual about whom an investigator conducting research obtains: (1) Data through intervention or interaction with the individual or (2) Identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, vein puncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject.”

Awardee institutions “engaged” in human subjects research in Qatar, must obtain an Assurance with the SCH, and establish appropriate policies and procedures for the protection of human subjects. An institution is engaged in human subjects research if:

1. the institution’s employees or agents intervene or interact with human subjects for research purposes;
2. the institution’s employees or agents obtain individually identifiable private information about human subjects for research purposes; or
3. the institution receives a direct QNRF award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

Certain research activities are exempt from regulatory requirements for an Assurance and IRB oversight. SCH Regulations state that institutions must adopt clear procedures under which the IRB (or some authority other than the investigator) determines whether proposed research is exempt from the human subjects regulations.

Unless all research activities meet the criteria for one or more exemptions from the SCH Regulations, research involving human subjects may only be conducted under a QNRF award if the organization has a current SCH approved Assurance and provides certification that an Institutional Review Board (IRB)
registered under the specific Assurance has reviewed and approved the proposed activity in accordance with the SCH Regulations.

In accepting an award that supports human subjects research, the awardee institution assumes responsibility for all research conducted under the award, including protection of human subjects at all participating and consortium sites, and for ensuring that an Assurance and certification of IRB review and approval exists for each site before human subjects research may begin. When consultants are performing research involving human subjects on QNRF-funded projects, the consultant's institution must establish an approved Assurance.

Applications will be considered incomplete if they do not address the involvement of human subjects in the Research Plan of the application. If human subjects research is anticipated within the period of the award but plans for involvement of human subjects cannot be described in the application, applicants must provide a detailed explanation why it is not possible to develop definite plans. Prior to the involvement of human subjects the awardee must submit to QNRF for prior approval either (1) detailed information as required in the Research Plan of the application, and meet the Assurance and IRB certification requirements, or (2) if all of the research meets the criteria for one or more exemptions, identification of which exemptions(s) is/are applicable to the research, and a justification for the exemption with sufficient information about the involvement of human subjects to allow a determination that the claimed exemption is appropriate.

Awardees may not draw funds for research involving human subjects at any site engaged in non-exempt research for any period not covered by both an Assurance and IRB approval consistent with SCH Regulations.

1.1. Assurance Requirements

The SCH Assurance commits the institution to compliance with the requirements set forth in the Policies, Rules and Regulations for Research Involving Human Subjects (SCH Regulations), and the terms of Assurance. Each institution that is "engaged" in QNRF supported human subjects research conducted in Qatar must obtain an Assurance from SCH. (See: https://d2vcoob0ykg520b.cloudfront.net/app/media/2794).

Each legally separate entity must file its own Assurance even if the organization does not operate its own IRB and designates another IRB (registered with SCH and agreeing to the designation) for that purpose. Affiliated organizations or organizations that will serve as additional performance sites for the grant-supported research also must file an Assurance. It is the awardee organization's responsibility to ensure that all sites engaged in research involving human subjects have an appropriate Assurance and IRB approval consistent with the SCH Regulations. It also is the awardee's responsibility to comply with QNRF prior approval requirements related to the addition of sites not included in the approved application. No individual may receive QNRF grant funds for
non-exempt research involving human subjects unless the individual is affiliated with or sponsored by an organization that assumes responsibility for the research under an Assurance.

1.2. Certification of IRB approval

Awardees must provide a certification to QNRF that the research application has been approved by an appropriate IRB, consistent with the SCH Regulations. IRB approval must have been granted within 12 months before the budget period start date to be valid.

Certification of IRB approval may be filed during the prefunding procedures. QNRF would recommend that the IRB review the actual application or proposal for QNRF support to ensure that IRBs verify that all research described in the application or proposal is entirely consistent with any corresponding protocol(s) submitted to the IRB.

For further details regarding the QNRF requirements, see Appendix 1.

1.3. Reporting to Funding Agency and the Supreme Council of Health

Under the SCH regulations, awardee institutions must have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and QNRF any unanticipated problem involving risks to subjects to others (http://www.sch.gov.qa/app/media/29). Any IRB suspension or termination of approval must include a statement of the reasons for the IRB’s action and must be reported promptly to the investigator, appropriate institutional officials, and any supporting department or agency head. Awardee institutions must also file incident reports with SCH of unanticipated problems involving risks to subjects or others, serious or continuing noncompliance with the SCH Regulations or with the requirements or determinations of the IRB, and suspension or termination of IRB approval.

For more information regarding reporting to QNRF, see Appendix 1.

1.4. Instructions for Preparing the Regulatory Requirement Section in the Research Plan on Protection of Human Subjects

1.4.1. This section is required for applicants answering “Yes” to the question “Are human subjects involved?” on the QGrants Application channel.

If human subjects are involved in the project, choose the scenario that applies to your project, below, and follow the directions/answer the questions from the scenario that applies to your project. The responses must be cohesive and include sufficient detail to allow evaluation by peer reviewers and QNRF staff. This section should be a concise, complete description of the target population/source of materials and proposed procedures.
Failure to address the applicable scenario’s directions and requirements will result in the application being designated as incomplete and will be grounds for the QNRF to defer the application from the peer-review round. Alternatively, the application’s impact/priority score may be negatively affected. If the involvement of humans is indefinite, provide an explanation and indicate when it is anticipated that human subjects will be involved. Choose only the scenario that applies to your research project. Read all the information carefully. There is a 40 page limitation to the Research Plan; be succinct.

1.4.2. No human subjects involved

Proposed research does not involve human subjects; and does not use biospecimens or data collected from human subjects. **No section related to human subjects protection, risks, benefits, knowledge to be gained is necessary.**

1.4.3. Scenario A: No human subjects research proposed

Criteria

<table>
<thead>
<tr>
<th>Human Subjects:</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemption Claimed:</td>
<td>No</td>
</tr>
</tbody>
</table>

If proposed studies using human data or biological specimens do not involve human subjects, an explanation should be provided of why the proposed studies do not constitute research involving human subjects.

The explanation could include: a description of the source of the data/bio specimens and whether there is any intervention or interaction with the subjects in order to obtain the specimens and data; what identifiers will be associated with the human specimens and/or data; and who has access to subject identities, if any; the role(s) of providers of the data/biological specimens in the proposed research; and the manner by which the privacy of research participants and confidentiality of data will be protected.

Research that does not involve intervention or interaction with living individuals, or identifiable private information, is not human subjects research. Research involving the use of coded private information or biological specimens may not constitute human subjects research if the respective conditions of the Qatar Supreme Council of Health (SCH) Policies Regulations and Guidelines for Research Involving Human Subjects have been met (http://d13jic5e805ehy.cloudfront.net/app/media/24). Research that only proposes the use of cadaver specimens is not human subjects research because human subjects are defined as “living individuals”. Research that proposes observation of human subjects in public spaces, with no interaction or intervention, when human subjects will remain completely anonymous is not human subjects research.
1.4.4. Scenario B: Non-Exempt Human Subjects Research

Criteria:

Human Subjects: Yes
Exemption Claimed: No

Address each of the five points below; the responses to the five required points below must be cohesive and include sufficient detail to allow evaluation by peer reviewers and QNRF staff.

1.4.4.1. Risks to Human Subjects

a) Human Subjects Involvement, Characteristics, and Design

- Describe and justify the proposed involvement of human subjects in the work outlined in the Research Plan.
- Describe the characteristics of the subject population, including their anticipated number, age range, and health status, if relevant.
- Describe and justify the sampling plan, as well as the recruitment and the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special vulnerable populations. (see SCH Policies Regulations and Guidelines for Research Involving Human Subjects and what populations constitute vulnerable populations, and the relevant policies, at: http://d13jic5e805ehy.cloudfront.net/app/media/24).
- If relevant to the proposed research, describe procedures for assignment to a study group (randomization). As related to human subjects protection, describe and justify the selection of an intervention’s dose, frequency, and administration; OR the frequency and administration of the study drug, if any.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators performing the proposed research. Explain how data from the site(s) will be obtained, managed, and protected.

b) Sources of Materials

- Describe the research material obtained from living individuals in the form of specimens, records, or data.
- Describe any data that will be collected from human subjects for the project described in the Research Plan.
- Indicate who will have access to individually identifiable private information about human subjects.
• Provide information about how the specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.

c) Potential Risks
• Describe the potential risks to subjects (physical, psychological, financial, legal, or other) and assess their likelihood and seriousness to the human subjects.
• Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

1.4.4.2. Adequacy of Protection against Risks

a. Recruitment and Informed Consent
Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent (be brief and describe the consent process, i.e. informed consent using a written form; or waiver of consent; or waiver of documentation). If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.

Include a brief description of the circumstances under which consent will be sought and obtained, and the method of documenting consent. If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be included in the application.

b. Protections against Risk
Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data.
Research involving vulnerable populations, as described in the Qatar Supreme Council of Health Policies, Rules and Regulations for Research Involving Human Subjects, must include additional protections. Refer to Qatar Supreme Council of Health regulations as follows:
• Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (p. 11): http://d13jic5e805ehy.cloudfront.net/app/media/24
• Additional Protections Pertaining to Biomedical and Behavioral Research Involving Vulnerable Subjects (p. 13): http://d13jic5e805ehy.cloudfront.net/app/media/24
1.4.4.3. Qatar Supreme Council of Health Requirements for Human Stem Cell, Gene Therapy and Clinical Research

- **Human Stem Cell Research**

  All proposed human stem cell research reviewed and approved by Institutional Review Boards (IRBs) must obtain approval by the Qatar Supreme Council of Health’s Recombinant DNA Advisory Committee prior to receiving funding and initiation of the studies. See SCH requirements for human stem cells research here: [http://www.sch.gov.qa/app/media/30](http://www.sch.gov.qa/app/media/30)

- **Gene Therapy**


- **Clinical Research**

  SCH provides guidance to assist the investigators in preparing proposals for multi-component clinical research, and to help the SCH to follow the program’s yearly progress and to monitor the attainment of the program’s objectives. [http://www.sch.gov.qa/app/media/28](http://www.sch.gov.qa/app/media/28)

  Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a general description of the plan for data and safety monitoring of the clinical trials and adverse event reporting to the IRB, QNRF and others, as appropriate, to ensure the safety of subjects, as described in the Qatar Supreme Council of Health Policies, Rules and Regulations for Research Involving Human Subjects, section regarding Data and Safety Monitoring: [http://d13jic5e805ehy.cloudfront.net/app/media/24](http://d13jic5e805ehy.cloudfront.net/app/media/24)

1.4.4.4. Potential Benefits of the Proposed Research to Human Subjects and Others

  Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.
1.4.4.5. Importance of the Knowledge to be Gained

Discuss the importance of the knowledge gained or to be gained as a result of the proposed research; and why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

1.4.4.6. Data and Safety Monitoring Plan (for biomedical research projects only)

Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB); and, when required to the Qatar Supreme Council of Health,[see Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, at http://d13jic5e805ehy.cloudfront.net/app/media/29]

The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by:

a. The Principal Investigator on the IRB application (required);
b. The Institutional Review Board (IRB) (required);
c. An Internal Committee or Board with explicit guidelines;
d. A Data and Safety Monitoring Board (DSMB) when required according with the Qatar Supreme Council of Health regulations “Monitoring Boards for Data and Safety” [http://d13jic5e805ehy.cloudfront.net/app/media/24].

1.4.5. Scenario C: Human Subjects Research Claiming Exemption 1, 2, 3, 4 and 5

Criteria:

Human Subjects: Yes
Exemption Claimed: 1, 2, 3, 4 and 5

Be succinct.

The exemption categories can be found in the Qatar Supreme Council of Health “Policies, Rules and Regulations for Research Involving Human Subjects” available at [http://d13jic5e805ehy.cloudfront.net/app/media/24].

Although the research may be exempt from the regulatory requirements, it is still research involving human subjects. Include the following statement: “This Human Subjects Research falls under Exemption(s) …” Clearly identify which exemption(s) (1, 2, 3, 4, and 5) you are claiming and justify why the research meets the criteria for the exemption(s) that you have claimed.
List any collaborative sites where exempt human subjects research will be performed, and describe the role of those sites and collaborating investigators performing the proposed research. Explain how data from the site(s) will be obtained, managed, and protected.

1.4.6. Scenario D: Delayed-Onset Human Subjects Research

Criteria:

Human Subjects: Yes
Exemption: Yes or No

Applications may be submitted with the knowledge that human subjects will be involved during the period of support, but plans are indefinite and it is not possible to describe the involvement of human subjects in the application (see Qatar Supreme Council of Health “Policies, Rules and Regulations for Research Involving Human Subjects”, section “Applications and proposals lacking definite plans for involvement of human subjects” [http://d13jic5e805ehy.cloudfront.net/app/media/24].

If the involvement of human subjects cannot be fully described, provide a detailed explanation why it is not possible to develop definite plans at this time. The explanation should be specific and directly related to the objectives in the application. If the involvement of human subjects depends upon information that is not presently available (e.g. completion of instruments, animal studies) be explicit about the information and the factors affecting the availability of the information, and describe what will be necessary in order to develop definite plans for the involvement of human subjects.

If an award is made, prior to the involvement of human subjects the awardee must submit to QNRF for prior approval either (1) detailed information as required in the Research Plan, Protection of Human Subjects (addressing risks to the subjects, adequacy of protection against risks, potential benefits of the proposed research, importance of the knowledge to be gained, and data and safety monitoring plan if applicable) and certification of IRB approval; OR (2) if all of the research meets the criteria for one or more exemptions, identification of which exemption(s) is/are applicable to the research, and a justification for the exemption with sufficient information about the involvement of human subjects to allow a determination that the claimed exemption is appropriate.

Under no circumstance may human subjects be involved in research until approval is granted by an IRB, and certification of IRB approval has been accepted by QNRF. [http://d13jic5e805ehy.cloudfront.net/app/media/24].
Section 2. Vertebrate Animal Research

2.1. Qatar Supreme Council of Health Requirements for Institutions Engaged in Research with Animals

The Qatar Supreme Council of Health (SCH) Policies, Regulations and Guidelines for Research Involving Laboratory Animals (SCH Policy) mandate that an approved Animal Welfare Assurance must be on file with SCH for institutions conducting research using live vertebrate animals. The SCH Policy requires institutions to establish appropriate policies and procedures to ensure the humane care and use of animals. The SCH Policy stipulates that the organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in research activities. This policy does not supersede institutional policies that impose more stringent standards for the care and use of laboratory animals.

In addition to a SCH-approved Animal Welfare Assurance, an awarded institution must provide verification that the Institutional Animal Care and Use Committee (IACUC) has reviewed and approved the proposed activity. IACUC approval must have been granted within three years to be valid. IACUCs are not authorized to administratively extend approval beyond three years. Verification of IACUC approval is requested before any animal research activities will be conducted.

Under collaborative institution agreements in which the awarded institution collaborates with one or more other organizations, the awarded institution, as the direct and primary recipient of QNRF grant funds, is accountable for the performance of the project, the appropriate expenditure of grant funds by all parties, and all other obligations of the awardee. The animal welfare requirements that apply to the awarded institution also apply to collaborating participants. The awarded institution is responsible for including these requirements in its agreements with collaborative institutions, and for ensuring that all sites engaged in research involving the use of live vertebrate animals have an approved Animal Welfare Assurance and that the activity has valid IACUC approval.

2.2. Instructions for Preparing the Regulatory Requirement Section in the Research Plan on Vertebrate Animals

2.2.1. This section is required for applicants answering “Yes” to the question “Are vertebrate animals involved?” on the QGrants Application channel.

“Animal” is defined as any live vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes. The generation of custom antibodies constitutes an activity involving vertebrate animals. If Vertebrate Animals are involved in the project, address each of the five points below; the
responses to the five required points below must be cohesive and include sufficient detail to allow evaluation by peer reviewers and QNRF staff. This section should be a concise, complete description of the animals and proposed procedures.

Failure to address the following five points will result in the application being designated as incomplete and will be grounds for the QNRF to defer the application from the peer review round. Alternatively, the application’s impact/priority score may be negatively affected. If the involvement of animals is indefinite, provide an explanation and indicate when it is anticipated that animals will be used.

If all or part of the proposed research involving vertebrate animals will take place at alternate sites (such as collaborative site(s)), identify those sites and describe the activities at those locations. There is a forty (40) page limitation for the Research Plan, so be succinct.

If an award is made, the awardee must submit to the QNRF detailed information as required in points 1-5 above and verification of IACUC approval prior to commence research involving vertebrate animals. If the awardee does not have an Animal Welfare Assurance then an appropriate Assurance will be required from the appropriate regulatory body of the jurisdiction where vertebrate animals will be involved in research.

**The five points are as follows:**

1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Strategy section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.

2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.

3. Provide information on the veterinary care of the animals involved.

4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.

5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the international recognized recommendations (e.g.: the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia). If not, include a scientific justification for not following the recommendations.
Performance site(s): The five points must be addressed for all performance sites (site where research with animals will be conducted).

- If the applicant’s institution is not where animal work will be performed, are all collaborative performance site(s) identified?
- If more than one performance site is planned, are descriptions of animal care and use addressing the five points provided for each site?

2.2.2. **Point 1: Describe the animals and their proposed use; address the following for all species to be used:**

- Species
- Strains
- Ages
- Sex
- Number of animals to be used

The description must include sufficient detail to allow evaluation of the procedures. Examples of the types of procedures that may be described include blood collection, surgical procedures, administration of substances, tumor induction and post-irradiation procedures.

2.2.3. **Point 2: Provide justifications for:**

- The use of animals
- Choice of species
- Number of animals to be used (cite power calculations, if appropriate) with specific justification for large numbers of animals
- Use of animals that are in short supply or are costly

LPIs must justify the use of animals in the proposed research. Before involving vertebrate animals, grantees should consider alternatives, such as mathematical models, computer simulation, and in vitro biological systems. The justification should indicate why alternatives to animals (e.g., computer models, cell culture) cannot be used and the potential benefits and knowledge to be gained. In addressing this point, researchers are encouraged to consider means to replace, reduce and refine the use of animals. Rationale for the choice of species must be provided (e.g., advantages of the species chosen and why alternative species are not appropriate). If less highly evolved or simpler animal models are available, justification should be provided for using more advanced species. For example, the use of dogs or cats should be thoroughly justified. If animals are in short supply, costly, or to be used in large
numbers, an additional rationale for their selection and the number of animals to be used is required.
Estimates for the number of animals to be used as accurate as possible; justification for the number of animals may include considerations of animal availability, experimental success rate, inclusion of control groups and requirements for statistical significance; cite power calculations where appropriate, must be provided.

2.2.4. **Point 3: Provide a general description of veterinary care, including veterinary support that is relevant to the proposed procedures. Examples of the kinds of items that may be appropriate to include are:**

- A brief account of veterinary staff and their availability
- The regular schedule of monitoring of animals by veterinary staff
- Any additional monitoring and veterinary support that may be required to ensure humane care, if relevant to the procedures proposed (e.g., post-surgical)
- Indicators for veterinary intervention to alleviate discomfort, distress or pain, if relevant.

Descriptions of veterinary care should indicate the availability of veterinarians or veterinary technicians. For example, in the Vertebrate Animals document might include information regarding the number of veterinarians and veterinary technicians associated with the applicant institution and their proximity to the performance site(s). The frequency with which veterinary staff observe or monitor animals should also be stated.

If survival surgeries are proposed, descriptions of veterinary involvement or post-surgical monitoring may be described. For example, if animal use involves invasive approaches that might result in discomfort, distress or pain, the investigator may describe the indicators for veterinary intervention and the ways in which veterinary staff may intervene.

2.2.5. **Point 4: Describe procedures to minimize discomfort, distress, pain and injury to that which is scientifically unavoidable in the conduct of research. Examples of the kinds of items that may be appropriate to include are:**

- Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain or injury
- Procedures to alleviate discomfort, distress, pain or injury
- Identify (by name or class) any tranquilizers, analgesics, anesthetics and other treatments (e.g., antibiotics) and describe their use
- Provisions for special care or housing that may be necessary after experimental procedures
• Plans for post-surgical care, if survival surgeries are proposed
• Indicators for humane experimental endpoints, if relevant
• Describe the use of restraint devices, if relevant.

Procedures or circumstances that may result in more than momentary discomfort, distress, pain or injury should be identified. Methods to alleviate discomfort, distress or pain should be described. If pharmacological agents are used, the agent(s) may be specified by name or class. Any additional (e.g., non-pharmaceutical) means to avoid discomfort, distress, pain or injury may be briefly described. The manner, circumstances and duration of all post-surgical provisions and care may be described. If special housing is necessary following surgery or manipulations, the Vertebrate Animals document may describe these. If procedures (e.g., pharmacological or surgical) might lead to severe discomfort, distress, pain or injury, indicators for humane endpoints and euthanasia (e.g., severe infection, respiratory distress, failure to eat, tumor size) may be described. All of these issues are particularly important for survival surgeries. If multiple surgeries are proposed, these should be well justified and provisions to avoid any potential complications may be described. Describe how restraining devices will be used, if applicable.

2.2.6. Point 5: Describe methods of euthanasia:
• Describe the method(s) of euthanasia and rationale for selection of method(s)
• Indicate if the method is consistent with international guidelines for euthanasia for animals and specify which guidelines you follow.
• Provide a scientific justification for the choice of method if not international guidelines recommended.

The method(s) of euthanasia must be described and must comply with international guidelines for the euthanasia of animals. If the method(s) do not comply with the above referenced recommendations, the rationale and scientific justification for use of the method(s) must be provided. The indicators for euthanasia (i.e., termination of experiment or humane endpoints) may be stated. It is not sufficient to state simply that humane methods will be used that are consistent with the recommendations of international guidelines for the euthanasia of animals or the Institutional Animal Care and Use Committee (IACUC).

For an example from The U.S. National Institutes of Health on how to address the five points in Vertebrate Animal Research, please see Appendix 2.
Appendix 1: QNRF Requirements for the Certification and Assurance in Research Involving Human Subjects

I. Initial Review Certification (IRB approval letter for initial review) Requirements

The Institutional Review Board (IRB) final approval letter\(^1\) (approval letter for initial IRB review) should contain the following required information:

1. The date when the final approval letter was issued by the IRB office.
2. Title of the research study that was reviewed and approved by the IRB.
3. Name of the Lead Principal Investigator (LPI) approved by the IRB and responsible for the conduct of the study\(^2\).
4. A list of documents that were reviewed and approved by the IRB for the initial review, with the version that was reviewed and approved by the IRB. The list should include: the research study protocol; the consent form (if a request for waiver of consent; or waiver of documentation of consent were approved, please state so); recruitment materials, if any; any other materials that were reviewed and approved by the IRB during the initial review of the research study. QNRF reserves the right to access to and audit the IRB files.

Note: Recording the version of the research study protocol, consent form, and recruitment materials will help the research team, the regulatory body and funding bodies tracking the modifications of the above referenced materials after their initial review and approval; and making sure that all the modifications were approved by the IRB.

5. The type of review that was conducted by the IRB for a specific study:
   a. expedited review;
   b. full committee review (for greater than minimal risk research);
   c. exempt from IRB review\(^3\).

6. For expedited review and exempt research: the category of expedited review or exempt under which the IRB approved the expedited review request/granted the exemption.

7. For expedited review and exempt research: the name of the IRB Chair/designee who approved the expedited review request/granted the exemption.

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\(^1\) QNRF will collect (all) the IRB determination letter(s) from the submitting institution. The submitting institution must collect the IRB determination from all the submitting institution collaborators, domestic and/or foreign.

\(^2\) The Lead Principal Investigator of the grant is viewed by QNRF as the principal investigator on the IRB application and is the one responsible to receive all the IRB certifications from all her/his collaborators (for multi-site studies).

\(^3\) The IRB is the only regulatory body that may grant an exemption, according with the Qatar Supreme Council of Health’s regulations for research involving human subjects.
8. For research approved under expedited review or approved by the full committee (greater than minimal risk):
   a. the approval date;
   b. the expiration date.

II. **Continuing Review Certification (IRB approval letter for continuation)**

**Requirements**

1. Date when the continuation approval letter\(^4\) was issued by the IRB office.
2. Title of the research study that was reviewed and approved by the IRB.
3. Name of the Lead Principal Investigator (LPI) approved by the IRB and responsible for the conduct of the study.
4. A list of documents that were reviewed and approved by the IRB for the request for continuation review, with the version that was reviewed and approved by the IRB. The list should include: the research study protocol; the consent form (if a request for waiver of consent; or waiver of documentation of consent were approved, please state so); recruitment materials, if any; any other materials that were reviewed and approved by the IRB during the initial review of the research study.
5. New approval and expiration dates for the research study approved for continuation (for research approved under an expedited review category; or for research approved by the IRB full committee).

III. **Other required IRB determination letters:**

The Lead Principal Investigator responsible for the conduct of the study should notify QNRF, and include the IRB determination letter, when one or more of the following issues occur:

- a research proposal that received funding from QNRF is disapproved by the IRB;
- a serious adverse event that is unexpected, related or possibly related to participation in the study, and suggests that the research places subjects or others at a greater risks of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, and resulted in suspension of new enrollment by the IRB;
- a major study deviation\(^5\) that resulted in suspension of new enrollment by the IRB.

\(^4\) QNRF will collect the final approval letter only from the main awardee of the grant. It is the sole responsibility of the main awardee to collect the final IRB approval letters from all collaborators inside or outside Qatar.

\(^5\) Deviations may be classified as minor or major. The criteria for major deviations may vary but often include factors having a significant impact on consent, eligibility, treatment, reporting of toxicity, participant risk and safety, disease outcome, regulatory compliance and data quality. A major deviation
QNRF will hold the funding during the IRB suspension of new enrollment; if the IRB will suspend the study or the Lead Principal Investigator, QNRF will terminate the award and will take the appropriate steps based on the IRB determination letter.

IV. Qatar Supreme Council of Health’s IRB Certification and Assurance Requirements

QNRF strictly follows the Qatar Supreme Council of Health (SCH) regulations for research involving human subjects. SCH regulations state that “Under no condition shall research covered by (SCH) Policy be supported or conducted prior to receipt of the certification that the research has been reviewed and approved by the IRB.” According to the SCH regulations, institutions conducting research with human subjects in Qatar must have an assurance filed with and approved by the SCH.

All research conducted in Qatar must be reviewed and approved by an IRB “established in accordance with the requirements of (SCH) policy”.

In case the institution filling a request for assurance with SCH does not have its own IRB, the institution should contact one of the institutions with an established IRB in Qatar that conducts and reviews similar research as the institution filling the assurance request (e.g. a Social-Behavioral IRB for social-behavioral research).

SCH’s regulations require that the IRB listed on the institutional assurance should be adequate for the type of research conducted by the institution filling the assurance request; when reviewing a request for assurance, SCH will most likely look at “…the adequacy of the proposed IRB in light of the anticipated scope of the research activities and the types of subject populations likely to be involved…”.

may affect the outcome, analysis or interpretation of the study. A minor deviation is a deviation that does not affect the outcome, analysis or interpretation of the study and otherwise does not meet the definition of a major deviation but may still need to be described in publications. The cancer Biomedical Informatics Grid® (caBIG®).
Appendix 2: Example from The U.S. National Institutes of Health on how to address the five points in Vertebrate Animal Research.

“Vertebrate Animals Example (This VAS has been modified from the original. It addresses all five points concisely.)

Aims 1-3 will be addressed in vitro; Aim 4 will be addressed using a mouse model of ocular infection.

1. Female Balb/c mice will be used to determine if virions treated with enzyme can cause viral keratitis, and to test the in vivo efficacy of the test articles. The studies will require 700 mice, 4-6 wks old. Based on prior experience, 70 groups of 10 mice each will be required over 5 yrs to achieve adequate statistical power. Ocular infection is accomplished by scratching the cornea of anesthetized mice with a sterile needle and exposing the scarred portion of the cornea to inoculum. Test articles are applied directly to the scarified cornea as liquid or cream. Following inoculation and recovery, mice are monitored for 30 days. With the mice under anesthesia, the eyes will be examined at intervals, microscopically, and flushed with medium with 2% serum to determine viral titers. Thirty days post-infection, with the mice under deep anesthesia, the trigeminal ganglia are removed aseptically for viral assay, followed immediately by euthanasia.

2. The proposal is to study mechanisms for the prevention of ocular disease caused by viral infections, a leading cause of blindness in the US. Mice are needed for these experiments because no alternative in vitro model incorporates all elements of the mammalian ocular immune system; too little is known about this system for the development of computer simulations. Mice are a well-accepted model for studying viral keratitis, assessing the virulence of viral strains and testing the efficacy of antivirals. Mice provide several advantages: a) The murine ocular immune system is similar enough to that of humans to allow extrapolation of the results; b) Their small size allows the use of smaller amounts of drugs for testing; c) The entire mouse genome is known and easily manipulated genetically, allowing extension of the work in future genetic studies. Female mice will be used due to compatibility issues. Balb/c mice will be used because they have intermediate resistance to infection. ABC-4 knockout and ABC-4 test-strains will be used. For the enzyme study, we will use 4 treatment groups (enzyme-1, enzyme-2, enzyme-3, and mock treated virus) and different amounts of inoculum for each condition allowing a more accurate calculation as to the effect of the digestions on infectivity. For the test-article peptide study, we will use two formulations (one aqueous and one hydrophobic), test 4 different concentrations and also vary the treatment protocol. Two groups will receive a single dose of drug in each of the two formulations prior to the addition of virus to assess prophylactic activity. These groups will not receive any additional enzyme treatments. Two groups will be infected with virus and beginning 4 h post-infection, we will treat with each formulation and concentration 4 times daily for 7 days.
3. All mice are housed in the Animal Resources Center of the University. Animal housing rooms are under temperature and humidity control. The mice will not be subjected to water or food restrictions, and bedding material is placed in each cage. The facility is staffed by four full time veterinarians and six veterinary technicians; the veterinary staff is on site and a clinical veterinarian is available at all times. Animal care staff conducts routine husbandry procedures (e.g., cage cleaning, feeding and watering) and checks animals daily to assess their condition. Laboratory staff monitors mice when treatments are given, disease is scored or samples are collected for titering. The veterinary staff monitors mice in their home cages, weekly. If animals exhibit any indication of infection or distress, the veterinary staff confers with laboratory personnel to recommend appropriate antibiotics, analgesics or other pharmaceuticals. The veterinary staff may intervene or recommend euthanasia based on animal welfare concerns.

4. Mice will be anesthetized with isoflurane (3-5%) during the infection process, when treatments are administered and titer samples are collected. This eliminates the need for restraint devices and topical anesthetics that would interfere with the infection and disease process. For post-procedural pain relief, we will administer buprenorphine twice daily for the duration of the experiments (i.e., approximately 2 wks post-inoculation). Death is not an endpoint for the studies; the Balb/c strain was chosen because of its resiliency and resistance to this particular virus. Our goal is to avoid severe infections leading to death. Though unlikely, if an animal reacts severely, it will be euthanized, based on humane indicators (e.g., failure to groom or feed). These experiments involve no post-surgical survival animals.

5. All mice will be euthanized by cervical dislocation under isoflurane anesthesia. Isoflurane ensures that the mice are unconscious, while dislocation ensures quick death. This minimizes animal distress, is effective and efficient; it is consistent with the recommendations of the AVMA Guidelines for the Euthanasia of Animals."