Research Ethics: Principles and Procedures

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Is it Important??

In 2012, President of Hungary, Pal Schmitt, resigned from his post after allegation of PhD thesis plagiarism

Is it Important??

In 2020, A Chinese court has sentenced He Jiankui, the biophysicist who announced that he had created the world's first gene-edited babies, to three years in prison

Who are the key stakeholders in research?

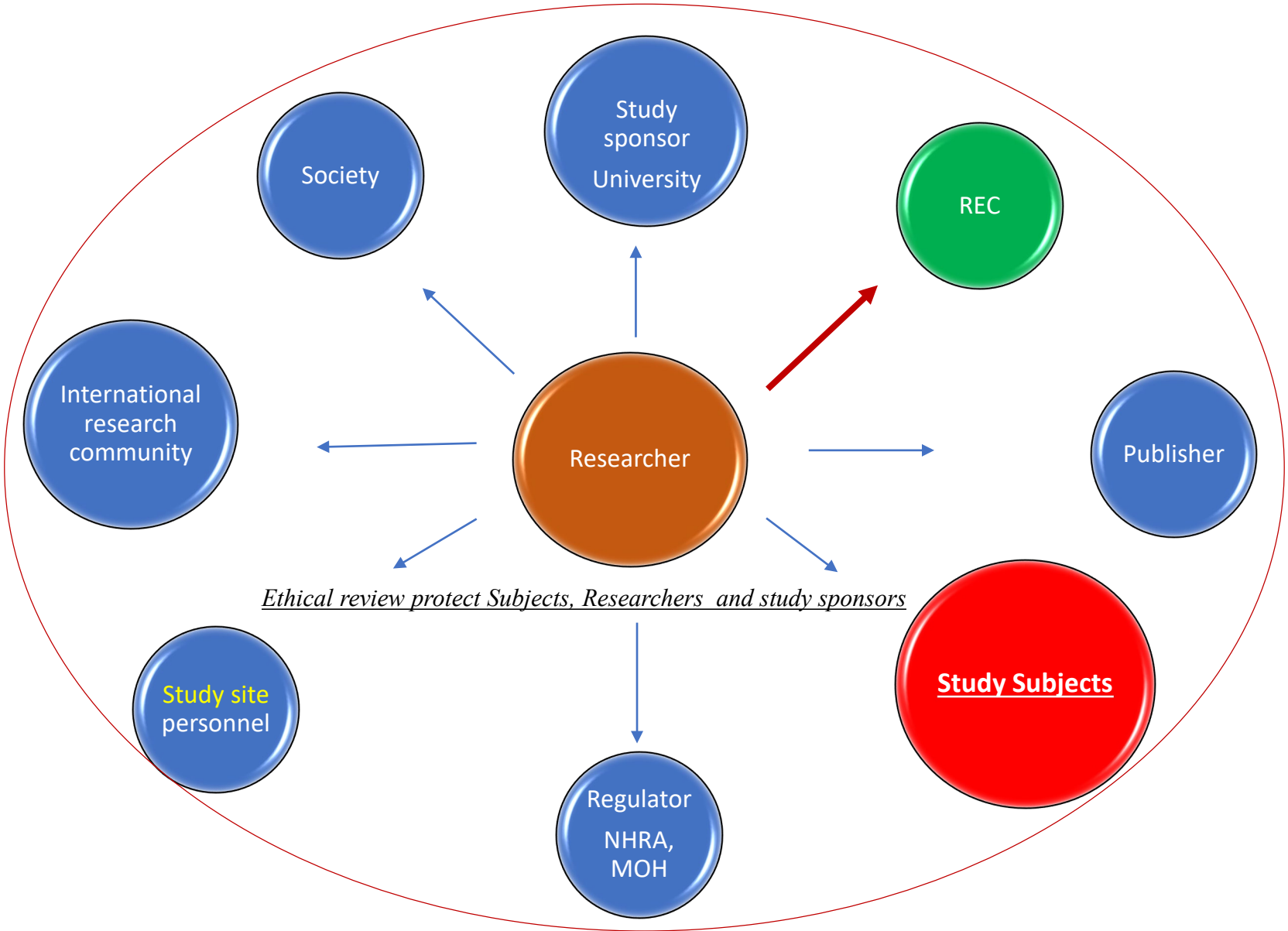


Table 1. Selected Guidelines on the Ethics of Biomedical Research With Human Subjects*

Guideline	Source	Year and Revisions
	Fundamental	
Nuremberg Code[35]	Nuremberg Military Tribunal decision in *United States v Brandt*	1947
Declaration of Helsinki[36]	World Medical Association	1964, 1975, 1983, 1989, 1996
Belmont Report[37]	National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research	1979
International Ethical Guidelines for Biomedical Research Involving Human Subjects[38]	Council for International Organizations of Medical Sciences in collaboration with World Health Organization	Proposed in 1982; revised, 1993
	Other	
45 CFR 46, Common Rule[8]	US Department of Health and Human Services (DHHS) and other US federal agencies	DHHS guidelines in 1981; Common Rule, 1991
Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products[42]	World Health Organization	1995
Good Clinical Practice: Consolidated Guidance[44]	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use	1996
Convention on Human Rights and Biomedicine[43]	Council of Europe	1997
Guidelines and Recommendations for European Ethics Committees[45]	European Forum for Good Clinical Practice	1997
Medical Research Council Guidelines for Good Clinical Practice in Clinical Trials[46]	Medical Research Council, United Kingdom	1998
Guidelines for the Conduct of Health Research Involving Human Subjects in Uganda[47]	Uganda National Council for Science and Technology	1998
Ethical Conduct for Research Involving Humans[48]	Tri-Council Working Group, Canada	1998
National Statement on Ethical Conduct in Research Involving Humans[49]	National Health and Medical Research Council, Australia	1999

*CFR indicates Code of Federal Regulations. More extensive lists of international guidelines on human subjects research can be found in Brody[39] and Fluss.[40] An extensive summary of US guidelines can be found in Sugarman et al.[41]

International Guidelines

Nuremberg Code (1947)

Between 1939 and 1945, at least 70 medical research projects involving cruel and, lethal experiments on human subjects were conducted in Nazi concentration camps

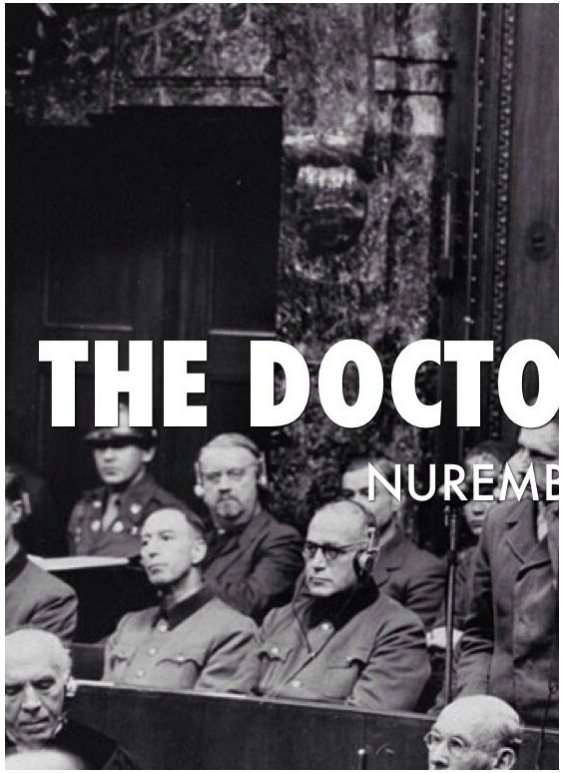
Breaking and re-breaking of bones (to see how many times they could be broken before healing failed to occur) Nazi

Belmont report (1979)

400 men had been left to suffer with syphilis long after a cure (penicillin) was available. (Tuskegee, Alabama, 1932-72)

Helsinki Declaration (WMA) (1964-2013)

- ✓ Established on September 18, 1947
- ✓ Has grown in 2018 to 113 national medical associations and more than 10 million physicians.
- ✓ Who is the Ceremonial Head of the WMA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NUREMB

Table 2. Seven Requirements for Determining Whether a Research Trial Is Ethical*

Requirement	Explanation	Justifying Ethical Values	Expertise for Evaluation
Social or scientific value	Evaluation of a treatment, intervention, or theory that will improve health and well-being or increase knowledge	Scarce resources and nonexploitation	Scientific knowledge; citizen's understanding of social priorities
Scientific validity	Use of accepted scientific principles and methods, including statistical techniques, to produce reliable and valid data	Scarce resources and nonexploitation	Scientific and statistical knowledge; knowledge of condition and population to assess feasibility
Fair subject selection	Selection of subjects so that stigmatized and vulnerable individuals are not targeted for risky research and the rich and socially powerful not favored for potentially beneficial research	Justice	Scientific knowledge; ethical and legal knowledge
Favorable risk-benefit ratio	Minimization of risks; enhancement of potential benefits; risks to the subject are proportionate to the benefits to the subject and society	Nonmaleficence, beneficence, and nonexploitation	Scientific knowledge; citizen's understanding of social values
Independent review	Review of the design of the research trial, its proposed subject population, and risk-benefit ratio by individuals unaffiliated with the research	Public accountability; minimizing influence of potential conflicts of interest	Intellectual, financial, and otherwise independent researchers; scientific and ethical knowledge
Informed consent	Provision of information to subjects about purpose of the research, its procedures, potential risks, benefits, and alternatives, so that the individual understands this information and can make a voluntary decision whether to enroll and continue to participate	Respect for subject autonomy	Scientific knowledge; ethical and legal knowledge
Respect for potential and enrolled subjects	Respect for subjects by (1) permitting withdrawal from the research; (2) protecting privacy through confidentiality; (3) informing subjects of newly discovered risks or benefits; (4) informing subjects of results of clinical research; (5) maintaining welfare of subjects	Respect for subject autonomy and welfare	Scientific knowledge; ethical and legal knowledge; knowledge of particular subject population

*Ethical requirements are listed in chronological order from conception of research to its formulation and implementation.

Main Principles

The 4 basic ethical principles that apply to all research are: Beneficence/ Nonmaleficence, Informed Consent , Autonomy, and Justice

Beneficence
Nonmaleficence

Informed consent

Autonomy

- Intentionality
- Understanding
- Absence of controlling influences that determine their action.

✓ Tell the truth.
✓ Respect the privacy of others.
✓ Protect confidential information.

Justice

•To each person an equal share
•To each person according to need
•To each person according to effort
•To each person according to contribution
•To each person according to merit.

(selection Criteria)

Special Communication

World Medical Association Declaration of Helsinki
Ethical Principles for Medical Research Involving Human Subjects

World Medical Association

Adopted by the 18th WMA General Assembly, Helsinki
29th WMA General Assembly, To
35th WMA General Assembly, Ve
41st WMA General Assembly, Hor
48th WMA General Assembly, Somerset West,
52nd WMA General Assembly, Edinbu
53rd WMA General Assembly, Washington, DC, USA
55th WMA General Assembly, Tokyo, Japan, Oct
59th WMA General Assembly, Seoul, Re
64th WMA General Assembly, Fort

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

CMMS Research Ethics Committee (REC)

Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants

WHO Library Cataloguing-in-Publication Data

Standards and operational guidance for ethics review of health-related research with human participants.

1.Research - standards. 2.Ethics, Medical. 3.Ethical review - standards. 4.Ethics committees. 5.Patient selection. 6.Guidelines. I.World Health Organization.

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World Health Organization

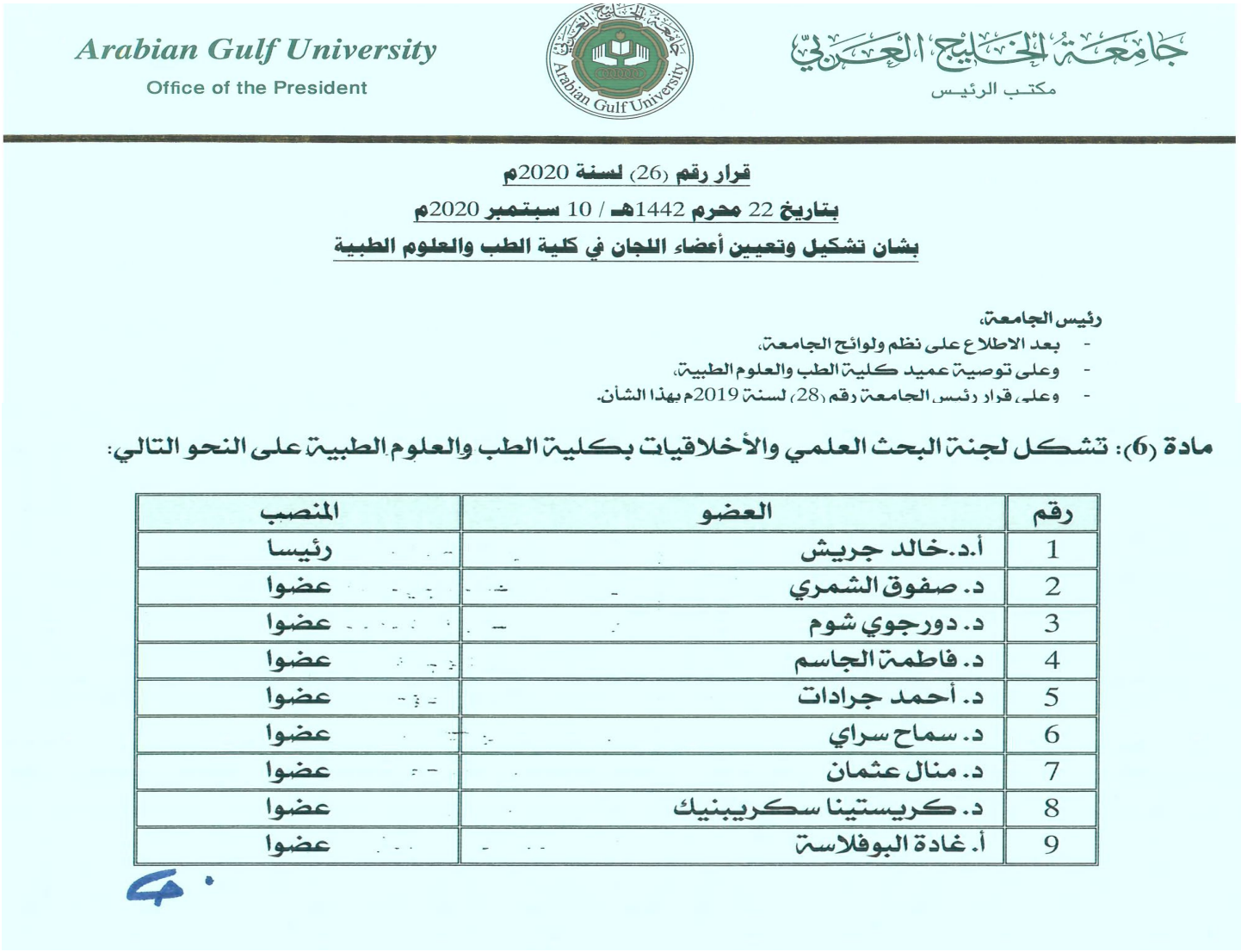
Standard 4: Independence of research ethics committees

Policies governing the REC include mechanisms to ensure independence of the REC's operations, in order to protect decision-making from influence by any individual or entity that sponsors, conducts, or hosts the research it reviews. Such policies provide at a minimum that REC members (including the Chair) remove themselves from the review of any research in which they or close family members have a conflicting interest.

To ensure that the REC cannot be pressured to approve or disapprove particular protocols, the charter, by-laws, policies and/or procedural rules of the REC provide that:

1. the REC's membership includes at least one person with no connection to the organization that sponsors or conducts the research under review;
2. researchers, sponsors, and funders may attend an REC meeting to answer questions about their research protocols and associated documents, but they are not present when the REC reaches decisions about their proposed research;
3. senior decision-makers of the entity creating the REC, or of any organization that sponsors or conducts the research reviewed by the REC (such as the director of an institution, or his or her agent), do not serve as members of the REC or its Chair;
4. the entity that establishes the REC ensures that REC members are protected from retaliation based on positions taken with respect to REC-related matters or review of research projects.

Members of CMMS REC for 2020-2021



Arabian Gulf University
Office of the President

جامعة الخليج العربي
مكتب الرئيس

قرار رقم (26) لسنة 2020م

بتاريخ 22 محرم 1442هـ / 10 سبتمبر 2020م

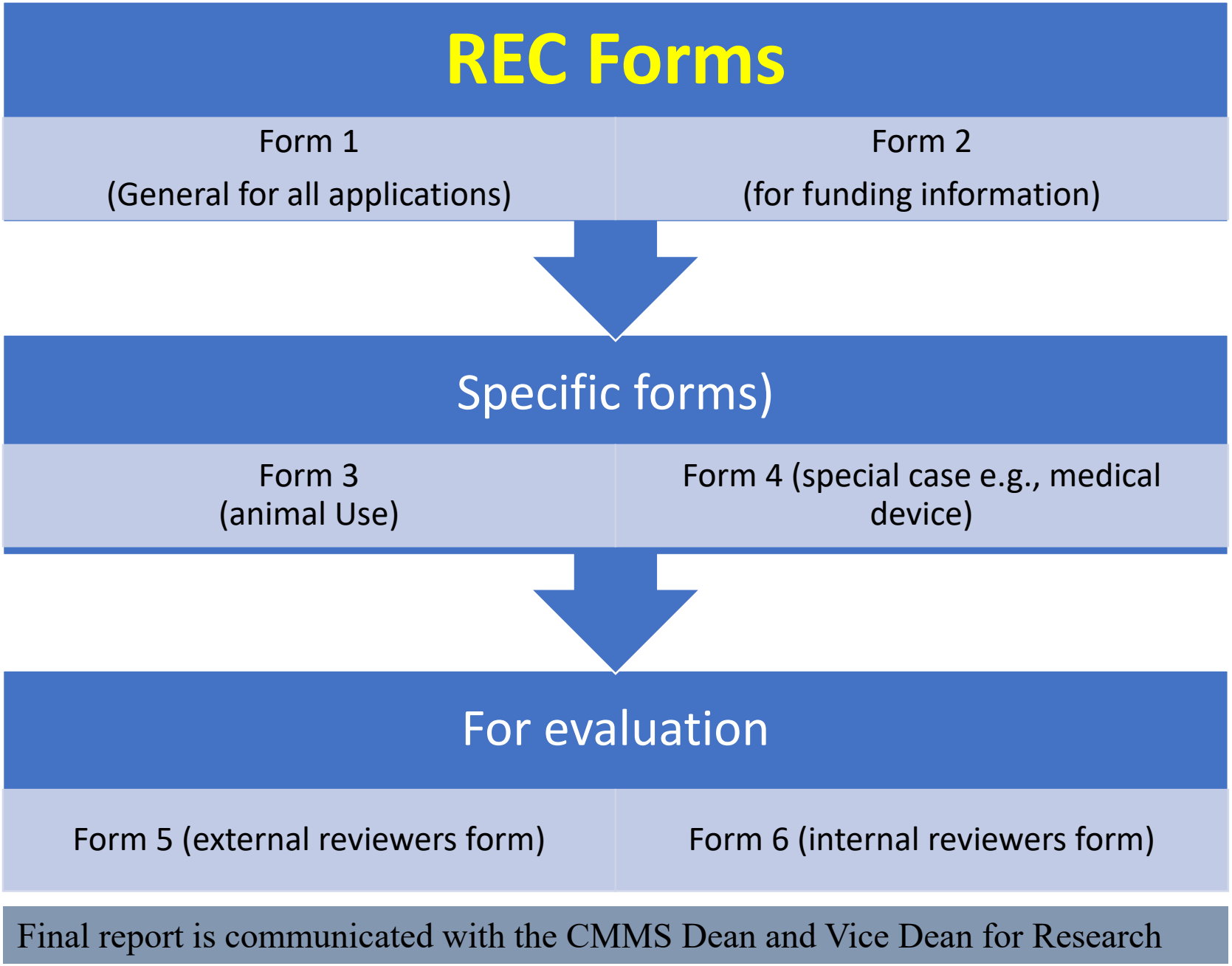
بشان تشكيل وتعيين أعضاء اللجان في كلية الطب والعلوم الطبية

رئيس الجامعة،

- بعد الاطلاع على نظم ولوائح الجامعة،
- وعلى توصية عميد كلية الطب والعلوم الطبية،
- وعلى قرار رئيس الجامعة رقم (28) لسنة 2019م بهذا الشأن.

مادة (6): تشكل لجنة البحث العلمي والأخلاقيات بكلية الطب والعلوم الطبية على النحو التالي:

رقم	العضو	المنصب
1	أ.د.خالد جريش	رئيسا
2	د. صفوق الشمري	عضوا
3	د. دورجوي شوم	عضوا
4	د. فاطمة الجاسم	عضوا
5	د. أحمد جرادات	عضوا
6	د. سماح سراي	عضوا
7	د. منال عثمان	عضوا
8	د. كريستينا سكريبنيك	عضوا
9	أ. غادة البوفلاسة	عضوا


REC Forms
Form 1
(General for all applications)
Form 2
(for funding information)
Specific forms)
Form 3
(animal Use)
Form 4 (special case e.g., medical device)
For evaluation
Form 5 (external reviewers form)
Form 6 (internal reviewers form)
Final report is communicated with the CMMS Dean and Vice Dean for Research

RESEARCH and ETHICS COMMITTEE (REC)
College of Medicine and Medical Sciences
Arabian Gulf University

APPLICATION FORM - Form (1)

Applicant name:		REC official Use Only:	
Staff number:		Reference number	
Student number:		Submission date:	

CHECK LIST FOR RESEARCH APPLICATION FORM

HAVE YOU:

- Submitted a hard copy of your application .....
- Submitted an electronic copy……
- Answered all questions .....
- Submitted a copy of the protocol .....
- Submitted all tools to be used in the study.....
- Submitted the informed consent form and patient information leaflet (H1).....

PART 1:
Principle Investigator (PI) information

1. Surname:	
2. First name:	
3. Telephone number	
4. Email:	
5. Academic title:	
6. Year of Dissertation and/or specialization, University or authority:	
7. Department (*Unit)*	
8. Undergraduate degree:	
9. Current position:	
10. Project period in years	
11. Signature	

REC Reference No. :

Section 1: Applicant and Participants

Institution/Department	
Address	
Telephone	
E-mail	
Principle investigator (Responsible User)	
Applicant(s)	
Participant 1	
Participant 2	
Participant 3	
Participant 4	
Application date	

Section 2: General Information

Working title		
Application category New experiments or continued experiments	☐ **New**	☐ **Continued**
Previous experience with comparable experiments		
Source of funding		
Planned dates	Start date:	End date:

Ethical Exemption

RESEARCH and ETHICS COMMITTEE (REC)
College of Medicine and Medical Sciences
Arabian Gulf University

APPLICATION FORM - Form 7 (Ethical Exemption)

Applicant name:		REC official Use Only:	
Staff number:		Reference number	
Student number:		Submission date:	

PART 1:
Principle Investigator (PI) information

1. Surname:	
2. First name:	
3. Telephone number	
4. Email:	
5. Academic title:	
6. Year of Dissertation and/or specialization, University or authority:	
7. Department (*Unit*)	
8. Undergraduate degree:	
9. Current position:	
10. Project period in years	
11. Signature	

Review Procedure

- ✓ Regular REC meetings takes place regularly every 3 weeks
- ✓ once the application received, it is filed and sent to all REC members
- ✓ The REC chair appoint 2 reviewers from the committee and ask them to respond within 10 days. All REC members can optionally send their feedback within the 10 days period.
- ✓ The REC reviewers (members) send their comments to the Chair and share their feedback with all members.
- ✓ After receiving the feedback, REC chair collate the feedback and communicate it to the applicant
- ✓ Once receiving the answers to comments from the applicant, the protocol is reviewed by the same REC reviewers in addition to the Chair or Vice Chair.
- ✓ the committee delegated the chair to issues ethical approval without discussion in the REC meeting if recommended by the reviewers and no objection from any committee member .
- ✓ If the feedback doesn't address the comments, the application is discussed in regular meeting for input from all members.

The average turn over of applications is 3 weeks from submission to approval

Documentation

No	Project No.	PI	Co-Investigators	Title of Study	Received date	Internal reviewer
1	E001-PI-10/20	Khalid Bindayna	Khaled Tabbara- Ronni Joji - Kassim Aradati - Haitham Jahrami - Shane Crinion - Hicham Ezzat	Genome Sequencing of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) strains prevalent in Bahrain	2-Oct-20	[redacted]
2	E002-PI-10/20	Tareq Alshaibani	Rima AbdulRazzaq- Yahya Naguib- Fuad Abdulla Ali	The Impact of the COVID-19 Pandemic on the performance of Medical Student in a Problem Based Learning System. A comparative Study Between face-to-Face and Virtual Learning.	5-Oct-20	[redacted]
3	E003-PI-10/20	Enas Darwish	Taysir Said Garadah- Ghada Hamad AL-Harbi -Sara Abdulaziz Khonji	Effect of using structured prebriefing on medical students' clinical judgement, competency, communication and self-satisfaction	5-Oct-20	[redacted]
4	E004-PI-10/20	Enas Darwish	Taysir Said Garadah- Ghada Hamad AL-Harbi -Sara Abdulaziz Khonji	Impact of using structured prebriefing on medical students' psychological safety and learning experience.	5-Oct-20	[redacted]
5	E005-PI-10/20	Rima Lutfi	xx	Online Instructional Methods of Cardiovascular Physiology to Medical Students during the Covid-19 Pandemic	11-Oct-20	[redacted]
6	E006-PI-10/20	Deeba Jairajpuri	Imtiyaz Hassan	Targeting SARS-CoV-2 main protease using natural compounds using screening, docking and molecular dynamics simulation	12-Oct-20	[redacted]
7	E007-PI-10/20	Abdelhalim Deifalla	Reginald Sequeira -Salah -Kassab Marawan Abu-Hijleh	Developing a framework to measure integration as a multi-dimensional construct in PBL medical curricula	13-Oct-20	[redacted]
8	E008-PI-10/20	Hasan M. A. Isa	Sebastien Taurin- Nora Abkal	Postnatal changes of the bacterial gut microbiome in newly born	14-Oct-20	[redacted]

How REC help researches ??

- Provide consultations regarding research methodology and research ethical conduct
- Assurance that research work meets international ethical guidelines
- Suggest scientific improvements to add value
- Help improve methodology
- Provide approvals to submit to regulatory agencies
- Provide approval to publish papers
- Document Researchers work and acknowledge contributor's work

Examples (case studies)

- Dr Greish want to use data from student records using student specific quotations (does this research need student's consent??)
- Dr Greish is planning to utilize a fatal acute condition new predictive test. The test is approved in Europe but not in Bahrain to start treatment at early time point. Can he keep the study results to see if the disease better predicted fatality than standard tests?
- Dr Greish is utilizing a validated questioner to test knowledge about STD:
  - Can he utilize the test without taking copyright permission?
  - Can he use the question in the questioner asking about the number of sex partners without modifications to suit the Arab culture?
- Dr Greish finished the research and after submitting the research article, he was asked to send the ethical approval number (which he did not obtain), then he sent to REC asking for a retrospective ethical approval.
- Dr Greish is applying for REC approval for the evaluating the knowledge of Bahraini population regarding XX. On ethical review, it was found the RCSI did the work on a larger sample size and published the data.
- Dr Greish want to use a sample size of 25 patients to detect gene variants that is reported in literature to have to be prevalent at 0.5% of population.
- Dr Greish is using a new off label technique to treat XYZ condition in his clinical practice, He wants to report the results of his practice in a research article.

FAQs

Why is the REC interested in issues of scientific validity or methodology?

- The Declaration of Helsinki (Sections 21 and 22) makes it clear that poor quality research is by definition unethical. This is because subjects are put through procedures and exposed to possible risk and resources are expended for no reliable gain in knowledge, or even the risk of erroneous "knowledge".

Do I need REC approval when I am conducting the study on another site with their own Ethics Committee?

- Currently, the accepted practise is to obtain REC ethical approval for all research to be published with CMMS affiliation as first, last or corresponding author.

Can I appeal REC comments regarding my application?

- Yes, you can appeal REC comments and REC chair can offer you to meet with REC members during regular meeting. In Rare case REC can invite external competent reviewers to review the application.

Does REC follow up to make sure applicants adhered to the written ethical approval?

- Yes, during the submission of progress report and final report of the project
- If the committee is asked to provide reviews regarding specific application

Can I modify my approved ethical approval?

- Yes, However, your protocol need to be amended accordingly and the modification reviewed by the REC for approval.