Section 1:

A. Research ethics committees (REC)

REC is a group of people appointed to review research proposals to assess formally if the research is ethical. This means the research must conform to recognised ethical standards, which includes respecting the dignity, rights, safety and well-being of the people who take part.

B. The importance and need for REC

Research is a core part of the university and it enables to improve the current and future health and well-being of the people they serve. However, research sometimes involves a degree of risk because researchers cannot predict the outcome with certainty. It may also involve additional burdens or intrusions exceeding those involved in normal care. Therefore, researchers must satisfy a research ethics committee, that is, the research they propose will be ***ethical*** and ***worthwhile***.

In this way, research ethics committees aim to protect people who take part in research. This helps to promote public confidence about the conduct of researchers and the dignity, rights, safety and well-being of research participants. As a result, more people will be encouraged to take part in research. This in turn leads to more, better and quicker improvements in health and social care.

C. Roles and responsibilities of REC

1. Protection of research participants

Whatever the research context, the interests of participants come first. Their dignity, rights, safety and well-being must be the primary consideration in any research proposal, as well as in REC review. RECs must be assured that there are proportionate safeguards to protect people taking part in research. RECs act primarily in the interests of research participants. The interests of researchers and research are always secondary to the dignity, rights, safety and well-being of people taking part in research.

2. Risk/benefits assessment

The committee should make an ethical assessment of the information provided in the application about the potential risks and benefits to participants and any measures in place to minimise the risks (e.g. rescue medication, stopping rules, emergency procedures, intensive care facilities). The ethical review must also ensure that the potential risks and benefits of the trial are fully and clearly explained in the participant information sheet.

RECs also take into account the interests and safety of the researchers, as well as the public interest in reliable evidence affecting health and social care, and enable ethical and worthwhile research of benefit to participants or to science and society.

3. Independence and impartiality

RECs are independent and impartial. A REC's opinion must be free, and must be seen to be free, from conflicts of interest. This includes freedom from pressures of institutional affiliation, profession-related interests, direct or indirect financial inducement, market forces, discipline- or topic-related bias.

4. Competence and efficiency

REC review must be competent, timely and authoritative. The membership and performance management of RECs, as well as the operational and administrative support they receive, are arranged to maximise the quality, rigour and promptness of REC review and the efficiency of their decision-making processes.

5. Compliance and enforcement

REC must adopt standard operating procedures approved by its appointing authority. In addition, REC ensure the compliance of the research with the standard applicable ethics. RECs must be assured about the planned ethical conduct and anticipated risks and benefits of any proposed research, however, they are not responsible for enforcement if the research turns out to be unsafe or is not carried out as agreed. This responsibility rests with the researcher, supervisor (if applicable) as

well as with the institution where the research takes place (or through which the researchers have access to participants, or their tissue or information).

6. Referral

RECs may seek advice from specialist referees on any aspects of an application that are relevant to the formation of an ethical opinion, and which lie beyond the expertise of the members or on which the Committee is unable to agree. These referees may be specialists in ethics, specific diseases or methodologies, or patients. Referees may be a member of another REC. However, when providing expert advice as a referee they are acting as an expert referee and not in their capacity as a REC member; the process for expert advice should therefore be followed.

7. Advice to applicants

RECs should take steps to facilitate communication with their potential or actual applicants. This includes advice about whether a proposed activity requires REC review, or the content, submission or review of an application.

D. <u>General requirements for submission of application</u>

1. An application for ethical review of a research study should be made by the Chief Investigator for that study.
2. Only one application for ethical review should be submitted in relation to any research protocol to be conducted.
3. All applications for ethical review to a REC should be submitted on the standard REC application form.
4. An applicant who requires general advice on the submission process or seeks advice on whether the study is suitable for review should contact REC only.
5. Research must not begin nor data can be collected/analysed before a **signed confirmation letter** is obtained from the Committee.

E. Validation of applications

1. The relevant period, within which an ethical opinion must be given, begins when a valid application is received by any REC. The validation date is the working day on which the complete application is received by the REC, including all relevant authorisations and all supporting documents.
2. It is the researcher's responsibility to ensure the completion of the application form accurately and send it, together with all related documents, to the REC in electronic and hard copies. Otherwise the application will be rejected.

F. Decision on validation

It is normally the responsibility of the receiving REC to decide whether or not the application is valid and to notify the applicant. Notification should normally be given within 15 working days of receiving the application by REC. An application should be accepted as valid if it has been correctly completed and submitted together with all supporting documents (electronic and hard copies). Please, note that submission of all relevant supporting documents that are indicated in the checklist are mandatory.

G. Revision of applications following submission

1. If the applicant considers it necessary to make significant revisions to the application form or the supporting documentation prior to review by the REC, he/she should withdraw the application.
2. Submission of a revised application form is required as part of a new application following withdrawal of a previous application.
3. It is appropriate for REC offices to request a revised application form when the initial application is invalid because the application form is incomplete or otherwise fails to meet the requirements of a valid application.

4. Where the REC raises questions about the content of the application form as part of its provisional opinion, applicants should provide any additional information, clarification or correction by letter.

H. Withdrawal of applications

If an applicant withdraws an application at any time, it should be recorded as 'withdrawn by applicant' and a clear reason should be provided by the applicant.

I. Research not requiring review by a REC

Responsibility for deciding whether research requires ethical approval rests with the REC. Where an application is received by a REC, that does not require reviewing and obtaining ethical approval, the applicant will receive a confirmation letter

J. Delayed applications

If applicant discloses that the research has already started without first obtaining an approval, the application should be considered invalid and the REC is not obliged to proceed with any form of ethical review. An ethical opinion cannot be given retrospectively.

K. Meeting schedules of REC

1. Meetings to review applications should minimally be held **once a month** except the vacation.
2. The closing dates for applications should normally be **14 days** prior to each REC meeting.
3. A REC should give its decision within **60 days** of receipt of a valid application. The sixty-day period excludes the time an applicant may take to supply additional information requested by the REC.

L. <u>Decisions available to the REC</u>

REC should reach one of the following decisions on any application reviewed at a full meeting:

- **Approval**

Un conditional approval is issued for the study when it raises no ethical concern.

- **Pending**

The Committee may decide that a final opinion cannot be issued until further information or clarification has been received from the applicant or a final opinion cannot be issued until further advice has been sought from a referee. The clock should be suspended from the date on which the request for further information was sent to the applicant. It should be re-started on the date when a complete response is received "the re-start date". The re-start date is the date on which a complete response is received in the REC office, not the date on which the information is considered by the REC and judged to be acceptable or otherwise.

- **Disproval**

Where the application is disproved, the applicant should be given a full explanation of the REC's reasons, clearly separated from any suggestions or comments made by the REC. The summary of ethical issues should set out the main issues considered by the REC in deciding on its opinion. The applicant should also be informed of the options available for further review.

M. <u>Amendments to research given an approval</u>

Where an approved research is undergoing an amendment, a notice (REC's amendment form) should summarise the change(s) included in the amendment and briefly explain the reasons in each case or refer to supporting documentation explaining the changes. One notice of amendment may refer to a number of different changes. The form should be completed in language comprehensible to a lay person and submitted with any relevant supporting

documentation, including the study protocol, which are clearly marked with the changes being made. If the changes listed are unclear, the amendment may be marked as invalid and further information requested.

A new application should only be required where a proposed amendment would **fundamentally** alter the nature of the research and the extent of the involvement of, or risk to, existing and/or potential participants. Examples might be where the proposed amendment involves:

1. A change in the primary purpose or objective of the research.
2. A substantial change in research methodology.
3. Introduction of new and substantially different classes of investigations or other interventions (rather than simply re-scheduling or modifying those already approved).
4. Recruitment of a new category of participant (especially if these would be regarded as being from vulnerable groups);

N. Appeals

Where REC has given a disproval, it is allowed for the applicant to send a written notice to REC that he/she wishes to appeal against the opinion and making representations. Such notice must be given within 60 days of being notified of disproval.

O. Serious breaches and protocol violations

The Chief Investigator is responsible for submitting all the related documents fully and accurately. The ethics committee may generally rely on the accuracy of this information. Protocol violations are non-compliances in relation to the protocol resulting from error or fraud/misconduct and identified as a “serious breach” by REC’s monitoring. A serious breach is defined as a breach of the protocol which is likely to affect to a significant degree the safety or physical or mental integrity of the participants or the scientific value of the research.

A report of breach may be provided by the Chief Investigator or by REC and it should give details of when the breach occurred, the location, who was involved, the outcome and any information given to participants. As a consequent of any serious breach, REC will invalidate the study.

P. Declaration of the conclusion or early termination of the research

If the study is terminated early, the applicant should notify the REC within 15 days of the date of termination. An explanation of the reasons for early termination should be given.

Q. Final report

A summary of the final report on the research should be submitted to the REC within 3 months of the conclusion of the research.

R. Renewal of approval

Ethical approval for Research Databases is given for the proposed study date, but may be renewed for further periods. The presumption is that approvals will continue to be renewed provided that the REC has adequate assurances of the continuing value of the resource and compliance with the terms and conditions of approval.

Section 2: Risk groups and laboratory biosafety levels

Risk groups are classified under four categories based on World Health Organisation guidelines:

- **Risk Group 1 (RG1)** agents have the lowest individual and community risk and include agents that rarely cause infection in healthy hosts. Some examples of RG1 agents: laboratory strains of non-pathogenic *E. coli*, *S. cerevisiae*, soil micro-organisms.
- **Risk Group 2 (RG2)** agents may cause disease in a healthy host but are difficult to transmit, don't usually cause serious or life-threatening illness and are readily treated or prevented.

Examples: pathogenic *E. coli*, *Campylobacter* spp, *Plasmodium* spp, prions, HIV (infected blood only).

- **Risk Group 3 (RG3)** agents are those that usually cause serious disease and may present a serious risk to laboratory workers. A Risk Group 3 agent may also present significant community risk if spread in the environment, but there are usually effective measures for treatment and/or prevention. Some examples: *B. anthracis*, hantavirus, yellow fever, HIV (cultures).
- **Risk Group 4 (RG4)** agents are those that present significant individual and community risks and usually produce life-threatening disease, are readily transmissible and effective prevention and/or treatment is not usually available. Examples: Ebola, Hendra and Nipah viruses.

Laboratory Biosafety Levels

Biological Safety Levels (BSL) are series of protections relegated to autoclave-related activities that take place in particular biological labs. They are individual safeguards designed to protect laboratory personnel, as well as the surrounding environment and community.

These levels, which are ranked from one to four, are selected based on the agents or organisms that are being researched or worked on in any given laboratory setting. For example, a basic lab setting specializing in the research of nonlethal agents that pose a minimal potential threat to lab workers and the environment are generally considered BSL-1—the lowest biosafety lab level. A specialized research laboratory that deals with potentially deadly infectious agents like Ebola would be designated as BSL-4—the highest and most stringent level.

These lab levels are determined by the following

- Risks related to containment
- Severity of infection
- Transmissibility

- Nature of the work conducted
- Origin of the microbe
- Agent in question
- Route of exposure

The reason biosafety levels are so important is because they dictate the type of work practices that are allowed to take place in a lab setting. They also heavily influence the overall design of the facility in question, as well as the type of specialized safety equipment used within it.

BSL–1

As the lowest of the four, biosafety level 1 applies to laboratory settings in which personnel work with low-risk microbes that pose little to no threat of infection in healthy adults. An example of a microbe that is typically worked with at a BSL-1 is a nonpathogenic strain of *E. coli*.

This laboratory setting typically consists of research taking place on benches without the use of special contaminant equipment. A BSL-1 lab, which is not required to be isolated from surrounding facilities, houses activities that require only standard microbial practices, such as:

- Mechanical pipetting only (no mouth pipetting allowed)
- Safe sharps handling
- Avoidance of splashes or aerosols
- Daily decontamination of all work surfaces when work is complete
- Hand washing
- Prohibition of food, drink and smoking materials in lab setting
- Personal protective equipment, such as; eye protection, gloves and a lab coat or gown
- Biohazard signs

BSL-1 labs also require immediate decontamination after spills. Infection materials are also decontaminated prior to disposal, generally through the use of an autoclave.

BSL–2

This biosafety level covers laboratories that work with agents associated with human diseases (i.e. pathogenic or infections organisms) that pose a moderate health hazard. Examples of agents typically worked with in a BSL-2 include equine encephalitis viruses and HIV, as well as *Staphylococcus aureus (staph infections).*

BSL-2 laboratories maintain the same standard microbial practices as BSL-1 labs, but also include enhanced measures due to the potential risk of the aforementioned microbes. Personnel working in BSL-2 labs are expected to take even greater care to prevent injuries such as cuts and other breaches of the skin, as well as ingestion and mucous membrane exposures.

In addition to BSL 1 expectation, the following practices are required in a BSL 2 lab setting:

- Appropriate personal protective equipment (PPE) must be worn, including lab coats and gloves. Eye protection and face shields can also be worn, as needed.
- All procedures that can cause infection from aerosols or splashes are performed within a biological safety cabinet (BSC).
- An autoclave or an alternative method of decontamination is available for proper disposals.
- The laboratory has self-closing, lockable doors.
- A sink and eyewash station should be readily available.
- Biohazard warning signs

Access to a BSL-2 lab is far more restrictive than a BSL-1 lab. Outside personnel, or those with an increased risk of contamination, are often restricted from entering when work is being conducted.

BSL-3

Again building upon the two prior biosafety levels, a BSL-3 laboratory typically includes work on microbes that are either indigenous or exotic, and can cause serious or potentially lethal disease through inhalation. Examples of microbes worked with in a BSL-3 includes; yellow fever, West Nile virus, and the bacteria that causes tuberculosis.

The microbes are so serious that the work is often strictly controlled and registered with the appropriate government agencies. Laboratory personnel are also under medical surveillance and could receive immunizations for microbes they work with. Common requirements in a BSL-3 laboratory include:

- Standard personal protective equipment must be worn, and respirators might be required
- Solid-front wraparound gowns, scrub suits or coveralls are often required
- All work with microbes must be performed within an appropriate BSC
- Access hands-free sink and eyewash are available near the exit
- Sustained directional airflow to draw air into the laboratory from clean areas towards potentially contaminated areas (Exhaust air cannot be re-circulated)
- A self closing set of locking doors with access away from general building corridors

Access to a BSL-3 laboratory is restricted and controlled at all times.

BSL-4

BSL-4 labs are rare. However some do exist in a small number of places in the US and around the world. As the highest level of biological safety, a BSL-4 lab consists of work with highly dangerous and exotic microbes. Infections caused by these types of microbes are frequently fatal, and come without treatment or vaccines. Two examples of such microbes include Ebola and Marburg viruses.

In addition to BSL-3 considerations, BSL-4 laboratories have the following containment requirements:

- Personnel are required to change clothing before entering, shower upon exiting
- Decontamination of all materials before exiting
- Personnel must wear appropriate personal protective equipment from prior BSL levels, as well as a full body, air-supplied, positive pressure suit
- A Class III biological safety cabinet

A BSL-4 laboratory is extremely isolated—often located in a separate building or in an isolated and restricted zone of the building. The laboratory also features a dedicated supply and exhaust air, as well as vacuum lines and decontamination systems.

Knowing the difference in biosafety lab levels and their corresponding safety requirements is imperative for anyone working with microbes in a lab setting.