TERMS OF REFERENCE FOR NATIONAL COMMITTEE ON ETHICS OF CELL RESEARCH AND THERAPY (NCERT)

1. CONSTITUTING THE COMMITTEE

The committee is constituted to ensure the competent review and evaluation of all ethical aspects of the research projects they receive and to ensure that their tasks can be executed free from bias and influence that could affect their independence.

The committee shall be multidisciplinary and multi-sectorial in composition, including relevant scientific expertise, balanced age and gender distribution, and laypersons representing the interests and the concerns of the community.

The committee shall be established in accordance with the existing policies of the country and in accordance with the values and principles of the communities they serve.

The committee shall establish publicly available standard operating procedures that state the authority under which the committee is established, the functions and duties of the committee, membership requirements, the terms of appointment, the conditions of appointment, the offices, the structure of the secretariat, internal procedures, and the quorum requirements. The committee should act in accordance with their written operating procedures.

1.1 Membership requirement

1.1.1 The Director General of Health shall appoint the chairperson among the committee members. The committee may also nominate individuals to be a committee member but it shall first be endorsed by the Director General of

Health. The Director General of Health may also revoke the appointment of members as and when required.

1.1.2 There will be a total of 18 members in the committee including the chairman but excluding the secretary. There must be at least one layman personnel in the committee, one member from the Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia, one member from the legal community, one representative from National Blood Centre, one representative from the university, and one representative from private sector.

The committee can form subcommittees to address specific and relevant issues that may arise.

There should be at least two members of any gender (male or female) in the committee.

1.1.3 Members must declare any conflict of interest including involvement in companies (especially related to stem cells) as well as any existing research on the subject.

1.2 Terms of appointment

1.2.1 The duration of the appointment shall be for a period of 3 years. The appointment may be renewed by the Director General of Health.

1.2.2 Members may disqualify themselves during meetings where there is a conflict of interest (e.g. a research proposal where the member is a principal investigator or a co-researcher).

1.2.3 Members may resign from the committee by submitting a letter to the Director General of Health and copied to the Chairman of the committee. The Director General of Health will then appoint the replacement member.

1.3 Conditions of appointment

1.3.1 All members shall give permission to publicize his/her full name, profession and affiliation.

1.3.2 All reimbursement for work and expenses, if any, within or related to the committee will be recorded and made available to the public upon request.

1.3.3 All members will sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants, and related matters.

1.3.4 All administrative staff in the committee will also sign a similar confidentiality agreement.

1.4 Offices

1.4.1 The office for the NCERT will be placed at the Medical Development Division, Ministry of Health, Malaysia.

1.4.2 The Director General of Health shall appoint the chairperson among the committee members. The chairperson will be nominated by the members of the committee and agreed upon by the Director General of Health who will then issue the letter of appointment.

1.4.3 The chairperson will be responsible for calling for meetings and chairing the meetings. In his/her absence the chairperson shall nominate a member from the committee to chair the meeting.

1.4.4 A secretary will be appointed by the Director General of Health and will be responsible for the notification letters to meetings, reminders to the meetings, minutes of the meeting, and drafting the decisions taken during the meetings.

1.4.5 The chairperson will sign the letter on behalf of the committee containing the decision of the committee with regard to the research proposal. All letters of approval will be accompanied by the attendance form signed by all members who attended the meeting.

1.5 Quorum requirements

1.5.1 The quorum for holding any meeting is 7 (seven) members. Meetings to discuss research proposals cannot proceed if the number of members present is less than seven.

1.5.2 A quorum must at least have a layman person (non-medical). The quorum should have at least 1 medical personnel. No quorum should consist of entirely members of one profession or one gender. A quorum should include at least one member whose primary area of expertise is in a non-scientific area.

1.6 Education for committee members

The members of the committee who are not familiar with the ethics and science of biomedical research as well as stem cell research and therapy will be provided with initial training and later continued education relevance to the subject of ethics and

biomedical science. Provisions will be made by the Ministry of Health to provide and sponsor members for opportunities for enhancing their capacity for ethical review. This education may be linked to co-operative arrangements with other ethics committees in the area, the country, and the region, as well as other opportunities for the initial and continued training of ethics committee members.

2. REVIEW

All properly submitted applications shall be reviewed in a timely fashion and according to the established review procedure.

2.1 Meeting requirements

2.1.1 The committee shall meet at least 3-4 times a year on scheduled dates that are announced in advance.

2.1.2 Additional meeting shall be planned according to the needs of the workload.

2.1.3 Members shall be given enough time in advance of the meeting to review the relevant documents.

2.1.4 Meetings shall be minute and there shall be an approval procedure for the minutes approved by the chairman.

2.1.5 The applicant, sponsor, and/or investigator may be invited to present the proposal or elaborate on specific issues.

2.1.6 Independent consultants may be invited to the meeting or to provide written comments, subject to applicable confidentiality agreements.

2.2 Elements of the review

All research related to cells and its derivatives in the country shall be submitted to NCERT through MREC for the process of review and approval.

The primary task of this committee is to review and ensure that every research carried out shall adhere to the related guidelines which include but not limited to National Guidelines for Stem Cell Research and Therapy, Guidance Document and Guidelines for Registration of Cell and Gene Therapy Product in Malaysia.

This committee will act as an independent body and shall not be influenced in decision making on any proposal submitted through the Medical Research and Ethics Committee, MOH or the Institutional Review Board (IRB) and / or the Institutional Ethics Board (IEB).

NCERT will act as a review committee to the Medical Research and Ethics Committee, MOH or the Institutional Review Board (IRB) and / or the Institutional Ethics Board (IEB) which are responsible for reviewing and giving approval for all research applications submitted to them. This committee will give recommendation to MREC/IRB/IEB with regard to the proposal. The monitoring process will be carried out by the respective review / ethics board and regular feedback to be provided to NCERT on regular basis.

3. DECISION MAKING

In making decisions on applications for the ethical review of the research, the committee shall take the following into consideration:

3.1 A member shall withdraw from the meeting for the decision procedure concerning and should be supported by clearly stated reasons. Application

where there arises a conflict of interest; the conflict of interest shall be indicated to the chairperson prior to the review of the application and recorded in the minutes;

3.2 A decision may only be taken when sufficient time has been allowed for review and discussion of an application in the absence of non-members (e.g. the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of committee staff;

3.3 Decisions shall only be made at meetings where a quorum (as stipulated in the ethics committee's written operating procedures) is present;

3.4 The documents required for a full review of the application should be complete and the relevant elements mentioned above should be considered before a decision is made;

3.5 Only members who participate in the review should participate in the decision;

3.6 Decisions shall be arrived at through a consensus;

3.7 Advice that is non-binding may be appended to the decision;

3.8 In cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed should be specified;

3.9 A negative decision on an application should be supported by clearly stated reasons.

4. COMMUNICATING A DECISION

A decision shall be communicated in writing to the applicant according to the committee procedures, within two weeks' time of the meeting at which the decision was made. The communication of the decision shall include, but is not limited to, the following:

4.1 The exact title of the research proposal reviewed;

4.2 The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable) on which the decision is based;

4.3 The names and (where possible) specific identification numbers (version numbers/dates) of the documents reviewed, including the potential research participant information sheet/material and informed consent form;

4.4 The name and title of the applicant;

4.5 The name of the site(s);

4.6 The date and place of the decision;

4.7 The name of the ethics committee taking the decision;

4.8 A clear statement of the decision reached;

4.9 Any advice by the committee;

4.10 In the case of a conditional decision, any requirements by the ethics committee, including suggestions for revision and the procedure for having the application re-reviewed;

4.11 In the case of a positive decision, a statement of the responsibilities of the applicant; for example, confirmation of the acceptance of any requirements imposed by the ethics committee ; submission of progress report(s); the need to notify the ethics committee in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the ethics committee in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form; the need to report serious and unexpected adverse events related to the conduct of the study; the need to report unforeseen circumstances, the termination of the study, or significant decisions by other ethics committee's; the information the ethics committee expects to receive in order to perform ongoing review; the final summary or final report;

4.12 The schedule/plan of ongoing review by the ethics committee;

4.13 In the case of a negative decision, clearly stated reason(s) for the negative decision;

4.14 Signature (dated) of the chairperson (or other authorised person) of the ethics committee.

5. FOLLOW-UP

The committee will follow the progress of all studies for which a positive decision has been reached, from the time the decision was taken until the termination of the research. The follow-up procedure should take the following into consideration:

5.1 The quorum requirements, the review procedure, and the communication procedure for follow-up reviews, which may vary from the requirements and procedures for the initial decision on an application;

5.2 The follow-up review intervals should be determined by the nature and the events of research projects, though each protocol should undergo a follow-up review at least once a year;

5.3 The following instances or events require the follow-up review of a study: a. any protocol amendment likely to affect the rights, safety, and/or well-being of the research participants or the conduct of the study; b. serious and unexpected adverse events related to the conduct of the study or study product, and the response taken by investigators, sponsors, and regulatory agencies; c. any event or new information that may affect the benefit/ risk ratio of the study;

5.4 A decision of a follow-up review should be issued and communicated to the applicant, indicating a modification, suspension, or termination of the ethics committee's original decision or confirmation that the decision is still valid;

5.5 In the case of the premature suspension/termination of a study, the applicant should notify the ethics committee of the reasons for suspension/termination; a summary of results obtained in a study prematurely suspended/terminated should be communicated to the ethics committee;

5.6 Ethics committees should receive notification from the applicant at the time of the completion of a study;

5.7 Ethics committees should receive a copy of the final summary or final report of a study.

6. DOCUMENTATION AND ARCHIVING

All documentation and communication of by the committee shall be dated, filed, and archived according to procedures. One individuals authorized by the committee can access and retrieve the various documents, files, and archives. All documents are archived for a minimum period of 3 years following the completion of a study. Documents that shall be filed and archived include, but are not limited to:

6.1 The constitution, written standard operating procedures of the committee, and regular (annual) reports;

6.2 The curriculum vitae of all ethics committee members;

6.3 A record of all income and expenses of the ethics committee, including allowances and reimbursements made to the secretariat and ethics committee members;

6.4 The published guidelines for submission established by the ethics committee;

6.5 The agenda of the ethics committee meetings;

6.6 The minutes of the ethics committee meetings;

6.7 One copy of all materials submitted by an applicant;

6.8 The correspondence by ethics committee members with applicants or concerned parties regarding application, decision, and follow-up;

6.9 A copy of the decision and any advice or requirements sent to an applicant;

6.10 All written documentation received during the follow-up;

6.11 The notification of the completion, premature suspension, or premature termination of a study;

6.12 The final summary or final report of the study.

SUBMITTING AN APPLICATION

1.1 Application

All applications for review of the ethics of the proposed stem cell research should be submitted by a qualified researcher responsible for the ethical and scientific conduct of the research.

1.2 Application requirements

1.2.1 All applications should be submitted to the: Secretary**,** MOH Research and Ethics Committee (MREC) or Institutional Review Board (IRB) or Institutional Ethics Board (IEB) of any universities

1.2.2 The format of the proposal is as per any standard scientific research proposal.

1.2.3 There is also a checklist for all stem cell research and therapy proposal.

1.2.4 The necessary documentation should be submitted together with research proposal. Research proposals shall be written in English.
Proposals should be submitted using a soft copy (CD) to the committee.

1.2.5 Only proposals submitted 4 (four) weeks before the committee meeting will be reviewed to give ample time for review by the members. Those submitted less than 4 (weeks) before the meeting will be reviewed at the subsequent meeting.

1.2.6 Proposals which are not complete will be rejected and notified by the secretariat.

1.2.7 Results of the review will be made available two weeks after the committee meeting.

1.2.8 All protocol amendments shall be submitted to the committee and investigators must await approval of the amendments before making the adjustments to their research or clinical trials.

1.3 Documentation

All the documentation required for a thorough and complete review of the ethics of proposed research should be submitted by the applicant. This may include, but is not limited to:

1.3.1 Signed and dated application form
The protocol of the proposed research (clearly identified and dated), together with supporting documents and annexes;

1.3.2 A summary (as far as possible in non-technical language), synopsis, or diagrammatic representation (‘flowchart’) of the protocol;

1.3.3 A description (usually included in the protocol) of the ethical considerations involved in the research;

1.3.4 Case report forms, diary cards, and other questionnaires intended for research participants;

1.3.5 When the research involves a study product (such as a pharmaceutical or device under investigation), 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);

1.3.6 Investigator(s)'s curriculum vitae (updated, signed, and dated);

1.3.7 Material to be used (including advertisements) for the recruitment of potential research participants;

1.3.8 A description of the process used to obtain and document consent;

1.3.9 Written and other forms of information for potential research participants (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;

1.3.10 Informed consent form (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;

1.3.11 A statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants;

1.3.12 A description of the arrangements for indemnity, if applicable;
A description of the arrangements for insurance coverage for research participants, if applicable;

1.3.13 A statement of agreement to comply with ethical principles set out in relevant guidelines;

1.3.14 All significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other ethics committees or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of modification(s) to the protocol made on that account. The reasons for previous negative decisions should be provided.

Reference:

WHO Operational Guidelines for Ethics Committees that Review Biomedical Research
(Published in 2000 by WHO, Geneva)