This document outlines the governance framework for human biomedical research (HBR), specifically the roles and responsibilities of parties which are involved directly in research, viz. the institution, the researcher and the institutional review board (IRB). All parties involved have a role to play in contributing to the overall responsibility for the ethical conduct of HBR that is shared by all parties.

**Existing Research Regulatory Framework**

2 The roles and responsibilities of various parties involved in human biomedical research are currently stated in the:

   (i) Medicines (Clinical Trials) Regulations;

   (ii) National Medical Ethics Committee (NMEC)’s ethical guidelines on research involving humans\(^1\);

   (iii) Bioethics Advisory Committee (BAC)’s reports\(^2\).

This document aims to consolidate those requirements into an over-arching governance framework.

**Regulatory Philosophy**

3 MOH intends to adopt a light-touch, risk-based approach such that research is not unnecessarily stifled, while still ensuring safety and well-being of research subjects. Regulatory requirements will be set for various types of research activities according to the level of ethical concerns, sensitivities and risks to patient safety and well-being, as what is appropriate for one type of research activity may be excessive or inadequate for another.

4 MOH’s role is to demarcate acceptable limits within which all human biomedical research should be conducted. The out-of-bound markers set clear prohibitions while allowing flexibility within boundaries. Within these boundaries, our preference is for self regulation. However, where necessary, MOH will not hesitate to exercise its enforcement powers to ensure that the safety and well-being of research subjects is protected. Benchmarks for ethical standards expected of various parties involved in research will also be set through guidelines or codes of practice.

**A) Role of Institutions**

5 Institutions have a public commitment to uphold the highest standards of human research subject protection, guided by internationally-accepted (e.g. the

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\(^1\) MOH required all government and restructured hospitals to establish ethics committees (or IRBs) in a circular dated 25 Jun 1998. These IRBs are required to comply with the NMEC guidelines.

\(^2\) MOH had issued a directive to all doctors in Jan 2006, informing that the BAC’s Reports will be used as the standard for ethical conduct in research in the evaluations and deliberations of the Singapore Medical Council.
Declaration of Helsinki and the Belmont Report) and local ethical standards. They are responsible for putting in place the necessary systems for ensuring the proper conduct of HBR and the protection of human subjects in all HBR carried out on their premises. Institutions also have the responsibility to ensure the proper access to, and use of, human biological material, medical records or other forms of personal information in their custody, for research.

6 The institution sets the tone for the culture of research within its organization and is responsible for complying with the relevant regulations and requirements related to HBR. Every institution involved in HBR should establish and maintain an effective IRB. The institution is responsible for the acts and decisions of the IRB(s) that it appoints. The institution is also responsible for:

(i) establishing the appropriate number of IRBs that is commensurate with the workload;
(ii) appointing qualified IRB members;
(iii) developing, documenting and regularly updating clear policies and procedures for the establishment and operation of its IRB(s);
(iv) providing adequate resources, e.g. protected time for its members and adequate administrative support, to enable each IRB to discharge its duties and responsibilities in a timely and effective manner;
(v) providing relevant education and training for IRB members. Such training and educational programmes should, where possible, also be provided to research staff;
(vi) providing IRB members (and members of committees that play a supporting role to IRBs, e.g. monitoring agents appointed by the institution such as a Data and Safety Monitoring Board) with full indemnity and arranging for the necessary insurance against any liability arising from their actions for members who act in good faith in discharging their duties;
(vii) putting in place a system to receive and manage feedback from research subjects (preferably through a one-stop direct access), with the power to investigate into the feedback, including anonymous ones. Mechanisms should be in place to protect the identity of persons providing feedback;
(viii) putting in place compliance monitoring systems to ensure that research is conducted in accordance with protocols approved by the IRB and applicable institutional standard operating procedures, relevant laws and other regulatory requirements; and
(ix) putting in place systems to ensure that researchers are familiar with the legal and ethical requirements for the types of research they intend to conduct and are appropriately qualified to conduct the research.

7 It is important for institutions to be aware of, and to recognise, any potential or apparent conflicts of interest at the institutional level, and take reasonable steps to avoid or minimise the conflict.
B) Role of Researchers

8 Researchers are responsible for conducting their research ethically and in accordance with the approved protocol. This is a non-delegable and personal responsibility of the researcher, i.e. it cannot be transferred or delegated to an IRB or to any party in the ethics review and governance process merely through the approval of a research project by an IRB.

9 Researchers must:
   (i) ensure that their research complies with all relevant laws and other regulatory obligations and requirements;
   (ii) comply with all other requirements of their institution and IRB that approved their proposals;
   (iii) fully disclose all other material facts and issues known to them (e.g. potential ethical difficulties or controversies and ethical reservations or doubts they hold) that might help the IRB carry out an impartial and objective review;
   (iv) maintain project and personnel oversight, and appropriately delegate research responsibilities;
   (v) inform and seek approval from the IRB for any proposed deviations from the terms of IRB approval for the project before its implementation;
   (vi) submit progress reports as required by their IRBs, as well as project completion reports and reports of adverse events within stipulated timeframes;
   (vii) maintain written documentation of activities for the required archive period;
   (viii) inform the subjects’ attending physician(s)\(^3\) about the subject’s participation in research that involves any level of clinical interaction with the treatment or management of patients for medical conditions relevant to the proposed research, if the physician(s) can be identified and if the subject agrees to the physician(s) being informed\(^4\). Clear arrangements should also be made with the attending physician for the researcher to ensure proper transfer of the responsibility of medical care of the subject in the clinical area under research to the researcher; and
   (ix) ensure that subjects are duly informed and clearly aware of any intended change in their treatment regimen. Researchers in such research studies which involve changes in clinical treatment regimen should be qualified physicians (or dentists, where appropriate) registered with the appropriate professional boards, and should be responsible for all research-related medical (or dental) decisions.

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\(^3\) The physician should be informed and given the opportunity to communicate his opinion and recommendation to the patient, prior to the commencement of the research.

\(^4\) Researchers are advised to be cautious and consider not enrolling subjects who do not consent to their attending physicians being informed.
10 It is important that researchers take special care to avoid any form of conflicts of interest in their research studies, whether actual, potential, or merely an appearance of conflict as such. Where such conflicts exist, researchers have a duty to declare, give a full disclosure of the facts giving rise to the conflicts, and detail the steps to be taken to minimise or avoid the conflicts.

11 In every research project, there must be one identified Principal Investigator (PI), who shall be the lead researcher of the project. If a single researcher is carrying out a research project, he or she shall be the PI. If multiple researchers are carrying out a research project, the researchers must among themselves designate a PI. In large research programmes, especially those with different parts or different (but related) objectives, or in which the research is to be carried out at multiple locations (i.e. multi-centre research), it is permissible to have multiple co-PIs, in addition to the PI. Even where several co-PIs are involved, the PI retains full responsibility. It is critical that one researcher, i.e. the PI, maintains full oversight of the project and be accountable for the conduct of the project. The exact roles and responsibilities of each of the other researchers in the team should also be made clear and documented in writing, especially in large, multi-part, multi-centre or complex research programmes.

C) Role of Institutional Review Boards (IRBs)

12 The IRB is a vehicle for an institution to implement its system of ethics governance of research carried out in the institution. The IRB acts on behalf of the institution that appoints it, and exercises, on its behalf, the authority and powers of that institution in matters within the terms of reference of the IRB. As IRBs play an integral role in the ethical governance of research, an IRB should report directly to the highest level of management of its appointing institution.

13 The IRB has a duty to ensure that all HBR carried out under the auspices of its appointing institution are ethically acceptable. The primary objective of the IRB is the protection and assurance of the safety, health, dignity, welfare and well-being of human research subjects. IRBs are responsible for:

(i) ethics review and approval of HBR projects;
(ii) continuing review, such as the evaluation of progress updates of research projects and adverse event reports provided by researchers, to ensure the continued validity of ethical approval of projects approved by them. IRBs should have the authority to suspend or terminate their approval of research projects where there are sufficient concerns over the safety and well-being of research subjects;
(iii) reporting to their respective institutions any unusual or unexpected events arising from the research in accordance with their standard

5 The Principal Investigator (PI) is the individual responsible and accountable for the design, conduct, monitoring, analyses and reporting of the protocol. The PI assumes full responsibility for the evaluation, analyses and integrity of the research data. The PI must ensure that the protocol is followed and the data collected promptly and accurately. The PI assumes specific responsibilities which include: writing the protocol document, ensuring that necessary approvals are obtained, monitoring the protocol during its execution, ensure that the protocol is conducted in accordance to the ethical guidelines, and to ensure that all participating investigators on the research teams involved in implementing the protocol are adequately informed about the protocol and their responsibilities.

6 Unusual or unexpected: As mutually agreed between IRBs and their appointing institutions.
operating procedures; and

(iv) providing feedback to, and maintaining dialogue about applicable
standards with, their constituent researchers.

Review of Scientific Merit

14 The IRB is not responsible for carrying out the scientific review of research projects. It is for the researchers to satisfy the IRB that an objective review of scientific merit has been carried out, and that the findings (whether positive or negative) of any review of scientific merit are made available and fully disclosed to the IRB. The IRB should be empowered to require a more extensive or rigorous review of scientific merit if deemed necessary.

Jointly appointed and shared IRBs

15 IRBs should not be appointed as ad hoc committees to consider research projects as and when they arise. Where, by reason of the small size of an institution or the small number of research projects arising from the institution, it is impractical to establish and maintain a standing IRB of its own, such an institution should make clear arrangements for its research projects to be considered by the IRB of a larger institution. The larger institution is allowed to charge a fee for such a service.

16 Alternatively, it is permissible for several small institutions to jointly appoint an IRB. These institutions will be held jointly accountable for the responsibilities expected of an appointing institution. There must be mutual agreement about, and documentation clearly detailing, the roles and responsibilities of each institution to ensure that there are no gaps in responsibilities.

17 Professional organizations, which by themselves do not conduct research (e.g. the Singapore Medical Association, College of Family Physicians Singapore), but whose members (e.g. General Practitioners) wish to conduct HBR, may set up standing IRBs to serve those members. In doing so, these professional organizations would have to take on the responsibilities expected of research institutions such that there will be no gap in responsibilities for the HBR projects reviewed and approved by their IRBs.

“Lead” IRB in multi-centre research

18 In multi-centre research, a “lead” IRB could be designated from among the IRBs of participating institutions. The lead IRB will conduct a full ethics review, coordinate the research programme, and keep other participating IRBs informed of any decisions and amendments made during the whole research period. The local portion(s) of a multi-national research project should be subject to review by the local IRB(s). Similarly, a “lead” local IRB may be designated where more than one local IRB is involved.

Impartiality and independence of IRBs

19 In the relationship between an institution and its IRB, the fundamental underlying principles are the independence of the IRB in the exercise of its powers and duties, and its ethical integrity. Therefore, although IRBs are appointed and supported by institutions, they owe a public and professional duty to act with total impartiality, objectivity and independence.
For the review of research projects, both IRBs and institutions alike must be aware of any potential or apparent conflict of interest involved and take reasonable steps to avoid and minimise the conflict.