

## **PART C: ETHICS GOVERNANCE**

### **SECTION IV: PRINCIPLES OF ETHICS GOVERNANCE**

#### **4. Principles of Ethics Governance**

##### **The Purpose of Ethics Governance**

- 4.1. Article 5 of the Helsinki Declaration states: "In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society." Article 8 of the Declaration states: "Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights."
- 4.2. Continuing human biomedical research is fundamental to improving our understanding of biological processes, and ultimately to the improvement of the health and welfare of humankind. Whereas diagnostic, prophylactic and therapeutic research have as their objective the immediate needs of individual patients, Human Biomedical Research has wider and longer-term objectives in the discovery of new knowledge that may lead to an improvement in the methods of diagnosis, prophylaxis and therapy of individuals, and to the health and welfare of society in general.
- 4.3. The experience of physicians in the management of patients often leads to new scientific insights, which when coupled with continuing human biomedical research leads to a virtuous circle that supports and advances biomedical knowledge to the benefit of both individuals and society at large. Article 4 of the Helsinki Declaration states: "Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects."

##### **Applicable Principles**

- 4.4. The fundamental objective of having a system of ethics governance in relation to biomedical research is to ensure the protection and assurance of the safety, health, dignity, welfare and privacy of human research subjects and to safeguard against research practices and objectives that are not ethically acceptable to society at that point in time.
- 4.5. But as with most kinds of diagnostic, prophylactic or therapeutic interventions, most forms of human biomedical research unavoidably

involve some degree of risk of harm (however minimal or remote) to the human subject.

- 4.6. Ethical assessment and judgment therefore necessarily involve an assessment and balancing of the potential harms and benefits. In general, human biomedical research should be directed towards the minimisation of risks and the maximisation of benefits, always bearing in mind the overriding considerations of the safety, health, dignity, welfare and privacy of the human subject and the ethical standards of society at that point in time.
- 4.7. To this end, a system of ethics governance must ensure that there is a proper assessment and weighing of the potential harms against the potential benefits of all human biomedical research, in accordance with the ethical values of the community. A proper system of ethics governance serves to strengthen public confidence in human biomedical research by ensuring that all forms of human biomedical research conform to the accepted body of ethical values of the community.
- 4.8. These fundamental ethical values are expressed and repeated in international documents such as the Declaration of Helsinki, the Nuremberg Code, the Belmont Report (“Ethical Principles and Guidelines for the Protection of Human Subjects of Research”, 1976), the UNESCO’s “Universal Declaration on the Human Genome and Human Rights” (1997) and the WHO’s “Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services” (1998).
- 4.9. In Singapore, these same principles are found or reflected in regulations such as the Medicines (Clinical Trials) Regulations, and in documents such as the SGGCP and the NMEC Guidelines. We have already addressed some of these principles at length in the Human Stem Cell Report and the Human Tissue Research Report.
- 4.10. These core principles are expressed, restated and elaborated upon in many ways. For example, the NMEC expresses some of these fundamental principles as follows:

*“2.3.1 The fundamental principle of research involving human subjects is respect for life. From this principle, others follow: that of beneficence, justice, and autonomy. Beneficence concerns the benefits and risks of participating in research. Justice relates to the fair distribution of risks in research in relation to the anticipated benefits for research subjects. Autonomy refers to the right of individuals to decide for themselves what is good for them.”*

- 2.3.2 *With respect to beneficence, the benefits and risks of research must always be carefully assessed. Research on human subjects should only be undertaken if the potential benefits arising from the expected new knowledge are of sufficient importance to outweigh any risk or harm inherent in the research, bearing in mind that risks and benefits may not be measurable on the same scale.*
- 2.3.3 *...Justice must be exercised in the allocation of the anticipated risks and the anticipated benefits...*
- 2.3.4 *A corollary of autonomy is that any research procedure must have, as far as possible, the free and informed consent of the experimental subject. Similarly, respect for the individual implies that safeguards should be provided to protect the experimental subject from physical and emotional harm including provisions for confidentiality.”*
- 4.11. Despite some uncertainty at the edges, a core of universally accepted principles and ethical values lie at the heart of most societies in their application to the protection of human research subjects.
- 4.12. In the interests of consistency and fairness of the judgments of IRBs, a code of applicable principles for ethics governance should eventually be formulated for the common guidance of IRBs, research institutions, researchers, the human research subjects and all other parties involved in human research.
- 4.13. We do not attempt, and it is beyond the scope of this document to attempt, to list all these fundamental principles. In our view, the applicable principles of the proposed code are best settled in an incremental and evolutionary manner through dialogue and discussion between IRBs and the other parties in the research governance process. This process of dialogue and discussion should be informed by and have reference to the experiences of the parties involved.
- 4.14. We take the view that it is part of the function of a responsive and dynamic system of ethics governance that the applicable body of ethics be reviewed and assessed from time to time to keep it relevant to and reflective of community values and the needs of research.
- 4.15. We emphasise that it is not the intention of this document to prescribe the specific ethical principles to be applied by IRBs and researchers in the process of ethics governance. We believe that these are professional

judgments that are appropriately and properly left to members of IRBs, researchers and other parties involved in the process of ethics governance.

- 4.16. We note, however, that certain broad ethical principles are universally accepted and applied in all the leading research jurisdictions. We find it appropriate and desirable for IRBs, researchers and other parties involved in the process of ethics governance to consider taking these ethical principles into account.
- 4.17. Such principles, in addition to or in elaboration of those identified by the NMEC, include:
- (a) Respect for the human body, welfare and safety, and for religious and cultural perspectives and traditions of human subjects. We elaborated on this principle in our Human Tissue Research Report. In the context of a diverse society such as Singapore, researchers have an especial obligation to be sensitive to religious and cultural perspectives and traditions of their human subjects.
  - (b) Respect for free and informed consent. This principle is discussed at length in our Human Stem Cell Report, our Human Tissue Research Report and the NMEC Report (Section 2.5). In addition, the Medicines (Clinical Trials) Regulations and the SGGCP recommend strict requirements regarding consent.
  - (c) Respect for privacy and confidentiality. This is treated in detail in Section 2.6 of the NMEC Guidelines and again in our Human Tissue Research Report.
  - (d) Respect for vulnerable persons. This is discussed in Sections 2.5.5 and 2.5.6 of the NMEC Guidelines. In essence, the ethics governance process must pay especial attention to the protection of persons who may not be competent to give consent themselves, or whose ability to give free and full consent may be compromised by physical conditions or other circumstances, such as being in a dependent relationship.
  - (e) Avoidance of conflicts of interest or the appearance of conflicts of interest. We further elaborate on this principle below in our discussion of the roles and responsibilities of researchers and IRBs.

## **SECTION V: INSTITUTIONAL REVIEW BOARDS**

### **5. Institutional Review Boards**

#### **The Role of Institutional Review Boards**

- 5.1. Ethics review bodies having the first responsibility for ethics review in the ethics review and governance process are variously known as “ethics committees”, “research ethics committees” or “institutional review boards”. In the context of Singapore, the term “ethics committees” is most commonly used.
- 5.2. We prefer instead the term “Institutional Review Board” (IRB). Our main reason for doing so is our desire to see institutional review boards established as full-time permanent supervisory bodies organised at and integral to the function of the highest administrative level in all institutions in which research is carried out. For instance, we think that institutional review boards in hospitals should be organised at the same level as medical boards, and that the institutional review board should report directly to the highest level of management of the hospital. We believe that the term “institutional review board” best reflects this role.
- 5.3. We differentiate here between IRBs that review, approve and supervise biomedical research involving humans, and hospital ethics committees that address issues arising out of clinical practice (clinical practice ethics committees). For the avoidance of doubt, we make clear that our recommendations in these Guidelines cover only IRBs that review, approve and supervise Human Biomedical Research, and are not intended to apply to clinical practice ethics committees.
- 5.4. We further clarify that the term "institution" is not limited to hospitals or medical clinics, but also includes any organisation or entity that carries out Human Biomedical Research as defined in these Guidelines. This includes commercial entities and government agencies.
- 5.5. We recognise that valuable Human Biomedical Research is also carried out by biomedical researchers who have no formal affiliation with IRB-guided institutions. Such biomedical researchers include medical practitioners in private practice (such as specialist consultants and general practitioners), and biomedical researchers who are employed by or who are affiliated with institutions that do not have and do not propose to constitute an IRB because of the low volume of Human Biomedical Research carried out by their employees or affiliates. In the case of registered medical practitioners and specialists in private practice, we suggest that they seek ethics approval for the conduct of their proposed research from the IRBs of

appropriate hospitals or other medical institutions. This approach could also be applied to biomedical researchers who are not registered medical practitioners. In any event, the requirements for appropriate ethics review as defined in these guidelines should apply regardless of the institutional affiliation of researchers.

- 5.6. There is universal agreement in all developed countries that IRBs are central to a proper framework of ethics governance of human research and that the primary objective of an IRB is to protect and assure the safety, health, dignity, welfare and well-being of human research subjects, in keeping with the principles outlined above.
- 5.7. Increasingly, collaborative research programmes are carried out across international borders (in multinational research programmes) or by researchers in several institutions (in multi-centre research programmes), or even a combination of both. It is usually a condition of such research programmes that the proposed or prospective researchers secure the approval of a properly constituted IRB in their own country or institution. Without a properly constituted IRB or access to such an IRB, an institution engaging in human research cannot hope to participate in such multinational or multi-centre collaboration research programmes.
- 5.8. From this viewpoint, the harmonisation of our national ethics governance framework with that in leading research jurisdictions is of national strategic importance.
- 5.9. The ultimate responsibility for the ethics compliance of human biomedical research rests with the researchers who carry out the research, and with the institution that sanctions the research or in which research is carried out.
- 5.10. The IRB is the vehicle through which such institutions act to implement a proper system of ethics governance of research carried out in such institutions.
- 5.11. We accordingly recommend that every institution that conducts Human Biomedical Research, or allows such research to be carried out on its premises, or on its patients, or involving access to or use of human tissue collections in its custody, or involving access to or use of medical records or other personal information in its custody, should establish and maintain an effective IRB.

### **Shared and Domain Institutional Review Boards**

- 5.12. Where by reason of the small size of the institution or the small number of research proposals it is impractical to establish and maintain a standing IRB of its own, such institutions should make clear arrangements with other institutions which maintain IRBs for research proposals to be considered by the IRBs of larger institutions.
- 5.13. Alternatively, it is permissible for several such institutions to jointly appoint a shared IRB.
- 5.14. Even in cases of institutions that already have their own IRBs, these institutions may prefer or wish to refer some kinds of research applications (for example, a proposal for research in a specialist area) to a specialist IRB or a domain IRB that has the technical capacity to assess research in that specialised area. Again, several institutions could jointly appoint and share in the expertise of such an IRB in situations where such expertise is limited. Such a specialist IRB has the advantage of delivering consistent decisions, special competence and knowledge in their field of specialisation.
- 5.15. We note that some hospitals and institutions in Singapore have set up domain specific IRBs with the intention of providing more focused and specialised ethics review. For example, sister or subsidiary institutions under the direction and control of a parent institution may choose to organise IRBs along domain lines, which can be shared by all the related institutions within the group. Such an arrangement is acceptable to us, as it is entirely in keeping with the ethical principles we have set out. Under this arrangement, the parent institution for all the hospitals and other institutions within the group will be responsible for constituting the necessary IRBs for all its constituent institutions and arranging for the accreditation of the IRBs.
- 5.16. We have no objections to other groups of research institutions adopting such a similar approach, provided that the terms of the arrangement between the institutions are clearly spelt out.
- 5.17. We therefore recommend that related institutions under the direction and control of a parent institution should be permitted to share an IRB or IRBs constituted by the parent institution.

### **The Responsibilities of Institutional Review Boards**

- 5.18. In its acts and decisions, and in the exercise and discharge of its duties and responsibilities, an IRB acts on the 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.
- 5.19. Accordingly, we emphasise that the institution is responsible for the acts and decisions of the IRB(s) that it appoints.
- 5.20. Ethics Review Gateway. The fundamental responsibility of an IRB is to act as an ethics review gateway for all Human Biomedical Research carried out under the auspices of its appointing institution, with the primary objectives of the protection and assurance of the safety, health, dignity, welfare and well-being of human research subjects. An IRB has a duty to ensure that all Human Biomedical Research carried out under the auspices of its appointing institution are ethically acceptable, and to comply with the principles outlined in Section IV.
- 5.21. Review of Scientific Merits. A review of the scientific merits of any proposed programme of Human Biomedical Research is an integral part of a proper assessment of the ethical acceptability of the programme. A research programme with little or no scientific merit is ethically unacceptable.
- 5.22. In its assessment of the ethical acceptability of any proposed research programme, an IRB will need to be satisfied that an objective review of the scientific merits of the proposed programme of research has been carried out, and that there is sufficient evidence of scientific merit before the IRB makes a decision on the ethical acceptability of the proposed research programme.
- 5.23. The IRB is not responsible for carrying out the scientific review of research proposals. 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 are fully disclosed to the IRB.
- 5.24. The review of scientific merits may be carried out by such committees, bodies or agencies as the IRB may in its judgment recognise as appropriate. Thus such reviews may be carried out by a scientific review committee constituted by the appointing institution or by the funding agency.

- 5.25. We note that it is an accepted practice for the initial scientific review to be carried out by or for the agency that funds the research. When the grant funding agency is satisfied with the scientific merits of the proposed programme of research, it then gives in-principle approval on the condition (among others) that ethics approval is granted by the appropriate IRB. In such cases, IRBs may rely on the review of scientific merits carried out by or for the grant funding agency, on the proviso that IRBs must make their own determination as to the sufficiency and adequacy of the review of scientific merits that has been carried out. In these cases, IRBs should be empowered to require a more extensive or rigorous review of the scientific merits if deemed necessary.
- 5.26. In addition, appointing institutions may give IRBs authority for:
- (a) Continuing Review and Supervision. The institution has an overall duty to ensure that approved research programmes are conducted in accordance with the terms of the approval. We elaborate on this responsibility in Section VII. IRBs may assist the appointing institution in the discharge of this duty, but such delegation will have to be made clear in the terms of constitution of the IRB. Such delegation should only be made if the IRB is given sufficient resources to carry out such a responsibility. In this responsibility, IRBs will require Principal Investigators (PIs) to submit annual (or more frequent) progress reports and final reports within three months of completion of projects. PIs will also have to inform and seek approval from IRBs for any proposed deviations from the terms of approval of the projects before they can be implemented except when they are necessary to eliminate immediate hazards to participants, or when the changes involve only logistical or administrative aspects of research, in which case IRBs should be informed within seven days. IRBs may also direct or otherwise require amendments or modifications to research proposals at any time, and to make such amendments or modifications a condition of approval for the conduct or continuation of the research programme.
  - (b) Reporting and Feedback. IRBs will require PIs to inform them of unusual or unexpected events within 15 days of occurrence and report such events to the appointing institutions. Another major aspect of the role of IRBs is to provide feedback to and maintain dialogue about application standards with their constituent researchers. In the discharge of their role, IRBs can and should also act as the key institutional agency that receives and reports to their appointing institutions on concerns and feedback expressed by research subjects.

- 5.27. The implementation of a framework for the work of IRBs has been laid down and discussed extensively by the NMEC in Section 3 of the NMEC Guidelines. We agree generally with the principles of implementation laid down by the NMEC, and further elaborate on these principles in our discussion of the constitution of IRBs below.
- 5.28. We therefore recommend that IRBs should have responsibility for the ethics review and approval of proposed Human Biomedical Research programmes on behalf of their appointing institutions. This should take into account the scientific merits of the proposed research.
- 5.29. Additionally, as institutional resources may permit, and on the mutual agreement of IRBs and their appointing institutions, IRBs may also be given authority by their appointing institutions for:
- (a) The continuing review and supervision (including evaluation of feedback from research subjects) of Human Biomedical Research programmes approved by them;
  - (b) The receiving of feedback from research subjects and the providing of feedback to researchers; and
  - (c) The reporting of unusual or unexpected events arising from the Human Biomedical Research programmes carried out under the auspices of its appointing institution to the management of that institution.

### **The Constitution of Institutional Review Boards**

- 5.30. IRBs should be established at the highest administrative level of the institutions. They should be appropriately resourced relative to the research activity of the institution and, where this is substantial, should be regarded as one of the key full-time management offices within the organisation of institutions, and not merely as honorary or *ad hoc* committees.
- 5.31. The IRB should be appointed by and report to at least an authority at the level of the Chief Executive Officer (as recommended by the NMEC Guidelines in the case of hospitals falling under the jurisdiction of the MOH pursuant to the Private Hospitals and Medical Clinics Act) or senior management.
- 5.32. IRBs should not be appointed as *ad hoc* committees to consider research proposals as and when they arise, although it is acceptable for institutions

with standing IRBs to appoint special *ad hoc* committees in consultation with their standing IRBs to consider special research proposals. We prefer, in such cases, that the institutions work with their standing IRBs to appoint special subcommittees co-opting experts or reviewers to assist the standing IRBs in the particular project concerned. For example, an IRB may receive a research proposal involving an area of research with which no member of the IRB is familiar. In such a case, the institution may work with the IRB to identify and co-opt *ad hoc* experts or reviewers to assist the IRB in its assessment and review of the proposal. The co-opted *ad hoc* experts or reviewers sit as a subcommittee of the IRB.

### Composition

- 5.33. We are of the opinion that the SGGCP (in particular Section 3.2.3) and the NMEC Guidelines (in particular Section 3.2.2) lay out appropriate and comprehensive guidelines regarding the composition of an ethics committee. We endorse these requirements and propose that they be similarly used to form the framework for the composition of an IRB.
- 5.34. In addition, we propose to highlight certain general requirements for the composition of an IRB:
- (a) Impartiality and objectivity are fundamental principles to be observed in the appointment of members to IRBs. An IRB should be carefully composed in order that there can be no room for any public perception that it is not independent of those who are required to submit to its review;
  - (b) Where a majority of the IRB members are drawn from within the appointing institutions, these persons should be the institutions' most senior, most respected and scientifically competent officers, researchers or consultants, who possess the appropriate experience and training;
  - (c) An IRB should include non-medical and/or non-scientific persons (lay representation) who are not members of or otherwise associated with the appointing institution of the IRB. Their inclusion is to reinforce the impartiality and objectivity of the work of the IRB;
  - (d) To further reinforce the independence of the IRB and to ensure that the decisions of the board are carried out in accordance with scientific thinking accepted within the community, external representation may include specialists of favorable reputation from other institutions; and

- (e) Lay representation may include respected lay members of the community and experts in philosophy, ethics, psychology, sociology or the law. The IRB may consult representative religious leaders on an *ad hoc* basis where it feels that such a need exists.
- 5.35. As far as possible, the core membership of an IRB should be representative of the particular fields of research carried out in the institution, such that for every research proposal received by the IRB, there will be at least one specialist or expert (and preferably more) on the IRB who may give a specialist viewpoint as needed.

### **Institutional Conflicts of Interest**

- 5.36. 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.
- 5.37. The research programmes that IRBs are asked to review are often of considerable financial or other benefit (potential or otherwise) to the appointing institutions. In the review of these research programmes, 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.
- 5.38. It is for this reason, among others, that we have recommended that IRBs report directly to the highest level of management of their institutions.
- 5.39. At minimum, all communications in relation to the review of the research programme in question should be fully documented in writing. Informal communication between the institution and its officers and the individual members of the IRB in connection with such research programmes should be strongly discouraged.
- 5.40. To facilitate greater understanding and in keeping with the ethical principle of informed consent, potential research subjects in Human Biomedical Research may need to be informed of any financial arrangements offered by corporate sponsors to researchers or their institutions (or both).
- 5.41. As part of its duty to make periodic reports, we recommend that IRBs include a special report on all reviews of research programmes in which there is an actual, potential or apparent conflict of interest. This special report should be made directly to the board of directors of the institution.

## **Multinational and Multi-Centre Research Projects**

5.42. As we have previously pointed out, biomedical research projects increasingly involve collaborators in more than one country. Indeed, one of the hallmarks of current leading edge research is the multinational and multi-centre collaborative nature of the research effort, which often involves a very large number of researchers based in many institutions in different countries.

### *Multinational Research Projects*

5.43. Guidance has been sought from us as to whether ethics review should be required for the portion of multinational research projects carried out in Singapore. We take the view that ethics review should indeed be required for any portion of a research project carried out in Singapore; or involving human tissue or medical, personal or genetic information collected in Singapore or derived from donors in Singapore; or which involves the export or transmission abroad of any human tissue or medical, personal or genetic information collected in Singapore or derived from donors in Singapore.

5.44. This conclusion is based on Singapore law and Singapore ethical standards and rules, which are not necessarily the same as those of other countries. This approach is supported in other jurisdictions. Without this approach a moral hazard would exist in the temptation of researchers to pick as their ethical jurisdiction of choice the jurisdiction with the perceived most liberal regime.

5.45. Nonetheless, we envisage that expedited review may be permissible in certain circumstances. For example, where human tissues from an IRB-approved study conducted in another country comes to Singapore for analysis, and the Singaporean institution does not have direct contact with the patient but merely performs tests on patient samples.

5.46. To avoid unnecessary bureaucracy, local research collaborators should be encouraged to provide their local IRBs with full documentation of ethics review applications made to the lead IRB (defined in paragraph 5.50), together with copies of all relevant queries and rulings of that IRB. If applications have been submitted or are proposed to be submitted to other IRBs in other jurisdictions, information on these applications and on their outcome, should be provided to the local IRB as well.

5.47. The local IRB may then elect to grant expedited approval of such applications after reviewing the documentation, and the reasons for the decision of the lead IRB. In general, local IRBs should consider a full

ethics review if a substantial portion of the research project is to be carried out in Singapore. Similarly, local IRBs should be concerned to ask for evidence of approval by IRBs in the jurisdiction in which the major part of the research project will be carried out.

- 5.48. In summary, we recommend that the local portion of a proposed multinational research programme should be subject to review by the IRB of the local partner institution or institutions.

*Lead IRBs for Multinational and Multi-Centre Research Projects*

- 5.49. Currently, the situation is that ethics review is required by the IRBs of every institution that will be involved in the proposed research programme. There is no mechanism or requirement that any one of the ethics committees involved should act as a principal or coordinating ethics committee.
- 5.50. We recommend that a “lead” IRB be designated from among the IRBs of the participating institutions. The lead IRB will be responsible for the primary ethics review of the research proposal and for keeping other participating IRBs informed of any decisions or amendments, including those made during the whole period of the research.
- 5.51. The choice of the lead IRB should be dictated by considerations such as the principal institution of affiliation of the PI, the location where the greater part of the research is carried out, the expertise of the constituted IRB, or the location where the largest number of subjects is located.
- 5.52. The primary ethics assessment should be made by the lead IRB, which is also responsible for ensuring that a proper scientific assessment has been carried out. Copies of its decision should be sent to the IRBs of the other institutions or organisations involved, which may then choose to conduct expedited review while reserving their rights to give further consideration to ethical and administrative aspects of the research that are specific to their own institutions or organisations.
- 5.53. Researchers should distinguish between core elements of their research (those components of their research that cannot be altered without invalidating the pooling of data from the participating institutions) and non-core elements (those that can be altered to comply with local IRB requirements without invalidating the research proposal).
- 5.54. At the time the research proposal is submitted, researchers should inform their respective IRBs as to which IRB is the designated lead IRB responsible for the primary ethics review.

- 5.55. Researchers are also expected to disclose to the lead IRB any previous decisions made by their IRBs regarding the research.
- 5.56. IRBs should:
- (a) Coordinate their review of multi-centre research proposals and communicate any concerns that they may have with other IRBs reviewing the project; and
  - (b) Determine how the conduct of multi-centre research will be supervised and the respective roles each of the institutions or organisations and their IRBs will have.
- 5.57. In summary, for multi-centre research, a “lead” IRB should be designated from among the IRBs of participating institutions. The lead IRB will play the main role in conducting a full ethics review, in coordinating the research programme and in keeping other participating IRBs informed of any decisions and amendments made during the whole research period.

### **Specific Operating Procedures for Institutional Review Boards**

- 5.58. Impartiality and independence. Although IRBs are appointed and supported by institutions, IRBs owe a public and professional duty to act with total impartiality, objectivity and independence in the discharge of their duties.
- 5.59. If for any reason a member of an IRB or the IRB itself should be of the view that there exist circumstances or considerations that might impair, adversely affect or make impossible the impartial, objective and independent discharge of duties, the member or IRB concerned should decline to review or process the research proposal or proposals in question and immediately report such concerns to the highest level of management of the institution.
- 5.60. Conflicts of interest. IRBs and members of IRBs should take especial care to avoid conflicts of interest, whether actual conflict, potential conflict, or only the appearance of conflict as such.
- 5.61. A situation of real, potential or apparent conflict of interest amounts to circumstances that adversely affects the impartiality, objectivity and independence of the IRB or of its members as described above.
- 5.62. In the event that a member of the IRB has a personal interest in the research under review, that member should recuse himself or herself from

any consideration of the case by the IRB, and he or she should refrain from offering his or her opinion to the IRB on the particular research under review.

- 5.63. The IRB member should make full disclosure of such an actual, potential or apparent conflict of interest to the IRB.
- 5.64. Fair review and documentation of decisions. IRBs should provide a fair hearing to those involved. Where there exist any doubts or difficulties with particular aspects of proposals, IRBs should clarify these in writing with the researchers, or in a minuted face-to-face meeting between the IRB and the researchers.
- 5.65. All discussions of the IRB should be appropriately minuted and all opinions recorded. The decisions of the IRB should be provided in written form and, where appropriate, a fair and frank account of the reasons for those decisions should be provided.
- 5.66. Ethics review by an IRB should be based upon fully detailed research proposals or, where applicable, the most up-to-date progress reports. The proposals or progress reports on which ethics review is based should be drawn up specifically for the purposes of submission for ethics review.
- 5.67. IRBs may also require the submission of a lay summary of the research proposal, where this may aid the lay members of the IRB in the conduct of ethics review. This summary should set out concisely the salient features of the research proposal. In certain cases, it may also be useful to have a lay summary of the scientific review.
- 5.68. Research proposals should not consist of the same or substantially the same documents submitted for the purpose of a proposal for funding. IRBs should bear in mind that research proposals submitted for ethics review are directed at a completely different end to that of proposals submitted for funding purposes.
- 5.69. The requirements of impartiality, fair review and documentation of decisions should apply equally to IRBs engaged in the continuing review or supervision of a research programme.
- 5.70. Free and Informed Consent. We recommend that the current statutory and legal requirements relating to the obtaining of free and informed consent of subjects in pharmaceutical trials should be applied to all other kinds of human biomedical research with appropriate modifications.

- 5.71. Both researchers and IRBs should take especial care to ensure that potential research subjects will be able to understand and assess the risks of participation, and that the consent-taking procedure and the documentation are properly designed to achieve this end.
- 5.72. Both researchers and IRBs should ensure that research participants are aware that they have the right to withdraw from the research programme at any time.
- 5.73. We recommend that IRBs and institutions formalise arrangements that allow participants a one-stop direct access to the full-time secretariat of the IRB or to a senior officer of the institution charged with quality service standards and control. In this way, research participants can have access to independent officers in order to give feedback on the research, or to express their concerns.
- 5.74. For related reasons, we further recommend that researchers consider appointing a member of their research team to serve as a one-stop participant contact. This contact person should be a registered medical practitioner or a senior member of the research team. It will be the responsibility of this person to handle initial contact in all cases in which a research programme involves any level of clinical intervention or interaction with the participants, and in cases where the interaction with participants is delegated to support and field workers or assistants (for example, the collation of medical histories or physical examination). We also recommend that IRBs make the appointment of a contact person a condition of approval.
- 5.75. A copy of every document signed by research subjects or given to them to read, including the consent documentation, should be retained by the research subjects.
- 5.76. The requirements for free and informed consent as discussed in our Human Stem Cell Report and our Human Tissue Research Report apply to the use of human biological materials in Human Biomedical Research.
- 5.77. Meetings. IRBs should have regular, formal, face-to-face meetings with a defined quorum. The work of the board should not be conducted routinely via circulation of documents. Applications that raise novel, unusual or difficult issues or those that present significant risk to participants should be debated and discussed in face-to-face meetings.
- 5.78. Exempted Review and Expedited Review. We have already discussed the basis for allowing Exempted Review and Expedited Review. When an institution (in consultation with its IRB) has decided on the categories of

Human Biomedical Research that could qualify for Exempted Review or Expedited Review, it should draw up a set of standard operating procedures to provide for these categories.

- 5.79. Instead of requiring consideration by the entire IRB, the standard operating procedures may allow the Chairperson or his delegate(s) to make decisions on applications that qualify for Expedited Review.

## **SECTION VI: RESEARCHERS**

### **6. Researchers**

#### **The General Responsibilities of Researchers**

- 6.1. Researchers share with institutions and IRBs a primary and central role in the ethics governance of Human Biomedical Research. More than any other party or parties in the ethics review and governance process, researchers have the fullest access to the facts on which ethical judgments are to be made.
- 6.2. Researchers are responsible for making the threshold decisions in conceiving, designing and putting together a proposed research project. In these decisions, they have the most freedom to shape the proposed research project in a way that gives fullest consideration and respect to ethical considerations, always cognizant of the fact that it is the human subjects whom they study who make their research possible, and are therefore under an obligation to respect and to protect the subjects.
- 6.3. IRBs therefore have to depend on researchers to make full material disclosure and give as full an account of the relevant facts as to enable them to make objective, impartial and fully informed ethical judgments.
- 6.4. Accordingly, the primary and ultimate responsibility for the ethical compliance of all aspects of the Human Biomedical Research rests with the researchers. IRBs bear the responsibility for the overall ethics review and approval of Human Biomedical Research programmes.
- 6.5. This responsibility of the researcher is a non-delegable and personal responsibility. It is a responsibility that 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 proposal by an IRB.
- 6.6. By the same token, researchers remain entirely responsible for ensuring that their research complies with all relevant laws and legal or regulatory obligations and requirements. Ethics approval given by an IRB is not to be taken as an assurance or representation by the IRB of such compliance, or as an assumption of legal liabilities arising out of the proposed research by the IRB. In short, it is unethical for researchers to treat IRBs and the review process merely as “legal insurers” or as “legal insurance”.
- 6.7. Researchers are primarily and ultimately responsible for making the first judgment as to whether, in their own professional judgment, the proposed research is ethical.

- 6.8. Researchers should only submit to IRBs proposals that they are objectively and professionally satisfied are entirely ethical in all aspects and are prepared to defend them as such.
- 6.9. By submitting a research proposal to an IRB, researchers indicate to all involved parties that the proposed research is, in the researchers' objective and professional judgement, ethical in all aspects.
- 6.10. Researchers should not submit to IRBs the same or substantially the same documents for ethics review that they submitted to prospective funding agencies, unless these documents focus on or evaluate the potential impact of the research on the safety, health, dignity, welfare and privacy of the subject in addition to solely describing the scientific merits of the research. However, we nonetheless prefer researchers submit a separate document for ethics review. Researchers should be aware that research proposals submitted for ethics review and research proposals submitted for funding purposes are directed at completely different ends and should be drafted accordingly.
- 6.11. In no circumstances should researchers use IRBs and the ethics review process as a means of gaining ethics approval for research projects that the researchers themselves entertain doubts or uncertainties about from the ethical point of view.
- 6.12. We recognise that there may be circumstances in which researchers may in good faith hold the view that the proposed research is ethical, but are nonetheless aware of differing opinions held in good faith by competent peers or an established body of public opinion, or that the proposed research may pose novel risks or other factors whose ethical implications may not be readily quantifiable or ascertained by them.
- 6.13. In such cases, we take the view that if researchers believe, in good faith, that the proposed research is ethical, then such proposed research may be submitted for ethics review *provided* that the researchers fully disclose all such differing opinions and potential ethical difficulties or controversies known to them; that the researchers fully disclose the ethical reservations or doubts they hold; and that researchers fully disclose all other material facts and issues that might help the IRB carry out an impartial and objective review. In such a process, where the researchers in good faith effectively assist the IRB in its attempt to explore all potential ethical issues, and to carry out an impartial and objective review of a novel situation, there is no objection to researchers submitting in good faith for ethics review a research proposal that the researchers themselves feel that they need ethical guidance.

- 6.14. It is important that researchers take special care to avoid any form of conflicts of interest, whether actual, potential, or merely an appearance of conflict as such. Where such actual, potential or apparent conflict arises, researchers have a duty to make a declaration of the conflict, to give full disclosure of the facts giving rise to such conflict and to detail the steps proposed or taken to minimise or avoid the actual or potential conflict of interest or the appearance of such a conflict of interest.
- 6.15. Researchers should not be involved in, or give the appearance of being involved in, the ethics review and approval process of any research project in which he or she is involved. For instance, a researcher who is a member of an IRB should recuse himself or herself from the review of any research project in which he or she is personally involved and make a declaration of such an interest to the IRB.
- 6.16. In submitting a proposal for ethics review, *every* researcher involved in the research project should be named as a party and applicant in the proposal.
- 6.17. For the purposes of this Section, we exclude from the definition of researcher, persons acting only in an administrative or support capacity and who have no independent control over the conduct of the research. Examples of such research support personnel would be administrative clerks and nurses assisting in clinical duties.

### **Principal Investigators**

- 6.18. Where a research project involves more than one researcher, the term “investigator” refers to any one of the researchers generally, while the term “Principal Investigator” specifically refers to the researcher who has been designated to undertake the role of Principal Investigator (PI) of that research project.
- 6.19. If a single researcher is carrying out a research project, then he or she shall be the PI. If multiple researchers are carrying out a research project, then the researchers must among themselves designate a PI. The PI is the researcher who shall be regarded as the lead researcher of the research project.
- 6.20. A research application by a group of collaborating researchers should be submitted in the name of a single PI and his or her collaborating researchers.
- 6.21. It is permissible for a research project to have more than one PI, especially for large projects, projects with different parts or different (but related)

objectives and projects in which the research is to be carried out at many locations (multi-centre research). Where more than one PI is involved, then each and every one of the PIs shall be held jointly and severally responsible as PIs.

- 6.22. PIs have special additional responsibilities over and above that of ordinary researchers.

The MOH has recently proposed a definition of “Principal Investigator” and of a PI’s roles and responsibilities:

*“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 assure that the protocol is followed and the data collected promptly and accurately. The PI assumes specific responsibilities to include: writing the protocol document, assuring 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.”*

- 6.23. We commend and adopt this definition and summary of the role and responsibilities of a PI, and extend it to all Human Biomedical Research as defined in these Guidelines.
- 6.24. We however also point out that in multi-centre, multinational trials of new drugs, there is often an international committee that designs and analyses the results of protocols. Thus, in the case of such pharmaceutical trials, the term “Principal Investigator” would apply to the appropriate and relevant person on that international committee, whether appointed to act as such or otherwise.
- 6.25. In large, multi-part, multi-centre or complex research programmes, it is especially critical that the exact roles and responsibilities of each of the researchers in a team should be made clear and reduced to writing. This makes clear to every researcher what each other’s responsibilities are, and helps identify overlooked areas requiring supervision or direction by a member of a team. Such statements outlining the roles and responsibilities of each of the researchers in a team should be included in the submission to the IRB.

- 6.26. The PI shall be responsible for settling, coordinating and formalising the distribution of roles and responsibilities among the researchers in a research programme.

### **Continuing Responsibilities, Deviation and Variation**

- 6.27. The ethical responsibilities of researchers outlined in this section are continuing responsibilities that apply at least for the lifetime of the research project, which is defined as the time the research project is submitted to the IRB for ethics review until the time the research project is deemed to have concluded or been terminated.
- 6.28. When an IRB approves a research application, its judgment is based on the facts and proposals disclosed to it by the researchers in their application. Most significantly, the ethical judgment has to be made *before* the research project begins. Once the project is approved and the research is underway, researchers may find that variations or departures from the original proposal may be dictated by such considerations as budget, access to subjects, unexpected clinical results and other factors. A research project may also expand in scope, in its objectives, or in the researchers involved. Some researchers may, for example, resign or take a less active role, while other researchers may be recruited. There are other situations in which deviation may occur. A proposed course of action may be found to pose greater risks for the proposed subject population than originally assessed, or that the research has resulted in greater harm (whether of degree or of incidence) than originally contemplated. Or it may be discovered in the course of the research that some part of the original protocol as proposed in the ethics review application has not been strictly adhered to, although such departure may have been made in good faith, by mistake or by necessity, out of consideration for the welfare of the subjects.
- 6.29. As part of his continuing responsibilities, the PI in particular is under a strict obligation to *immediately* and in writing seek approval for any changes where such changes have not yet been made, or otherwise report any changes where such changes have already been made, to the IRB by which the initial research application was considered and approved. The PI shall in his request or report detail the changes, giving his objective assessment of any impact and consequences (both from the clinical and ethical points of view) of the changes.
- 6.30. This continuing obligation of researchers is clearly referred to in the NMEC Guidelines (Section 3.2.5). The NMEC Guidelines state that investigators are “bound to act in exact accordance with the details” of the protocol submitted for ethics review and that investigators are “obliged to

report to the [IRB] any adverse events and apparent risks beyond those predicted in the original submission. The investigator should also immediately inform the [IRB] of any new information that might alter the ethical basis of the research programme. The [IRB] should also be notified if the study is terminated prematurely.” We agree entirely with the NMEC in these statements and adopt them.

- 6.31. The submission of a protocol operates as a representation and agreement by each researcher who signs the application that the research programme will be carried out strictly in accordance with the submitted protocol.
- 6.32. Researchers are obliged to suspend their research immediately, pending their report to the IRB, if deviations or changes to the original project submitted are substantial. Researchers are under the same obligation if deviations and changes have resulted or will likely result in greater harm or greater likelihood of harm (whether of degree or incidence) to the subjects involved.
- 6.33. Minor changes intended *solely* for the greater safety, health, welfare and well-being of the human subjects taken after consultation with all researchers involved in the research need not be immediately reported to the IRB. For example, if it appears to a researcher that a particular research subject is not altogether comfortable with one of the planned procedures, that procedure may be stopped and the research programme varied to such extent, without the need for immediate reporting. Reporting of such changes by the PI to the relevant IRB should however take place within a time frame that shall be decided by the IRB. We note, for example, that certain IRBs in institutions in the United States require such changes to be reported in annual updates. However, other changes, minor or otherwise, made for the greater effectiveness of the research or for meeting its objectives, do not fall within this category and should be immediately reported.
- 6.34. PIs have an obligation to submit regular reports to IRBs regarding the status of their research programmes. These reports are intended to aid the IRBs in its role of continuing review and supervision.

### **Researchers and Attending Physicians**

- 6.35. Human subjects for research projects are often recruited from patients who are already receiving treatment from physicians.
- 6.36. Where a proposed researcher is the attending physician, the researcher-physician should be aware of a potential conflict of interest and of the fact

that their patients may feel obliged to give consent. We repeat and endorse Article 23 of the Declaration of Helsinki, which states that:

*“When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.”*

- 6.37. In our view, however, this does not apply to situations where physicians wish to write up or publish summaries or analyses of the results of their therapeutic interventions or treatment of their patients, provided that such interventions and treatment were carried out in the first place purely for therapeutic or diagnostic purposes and in the interests of the patients and without regard to any consideration for research objectives or for the subsequent publication of the results.
- 6.38. In some circumstances, it may be difficult or impractical for researcher-physicians to comply with the letter of Article 23 of the Declaration of Helsinki. Such a situation might arise, for example, where the patient and prospective research subject is receiving specialist treatment at a centre or institution at which a majority of the attending physicians are also actively involved in institution-level research programmes. Or it may be that there is only one relevant specialist at the given institution, and that specialist is at the same time the treating physician as well as the proposed researcher. We recommend that in such cases, the IRB may give directions for the consent to be taken by the researcher so long as safeguards are documented in the protocol.
- 6.39. In the conduct of research programmes involving any kind of clinical or social interaction with human subjects who are receiving treatment for medical conditions, researchers should be aware of the possibility, however remote, that such interaction may have the inadvertent effect of interfering with the therapeutic care of the subject-patient.
- 6.40. Subject to our specific recommendations in paragraph 6.44, we therefore recommend that where researchers are aware that the potential research subjects are currently receiving treatment or otherwise being attended to by physicians for a medical condition or disease relevant to the proposed programme of research, efforts should be made by the researchers to inform and discuss with the attending physicians. If the research subject customarily attends a hospital or clinic and is attended to by different physicians on each visit, efforts should be made to inform the institution

concerned and to discuss with the consultant or a senior person having charge of the department or clinic.

- 6.41. We make clear that this obligation on the part of researchers, in those circumstances that it exists, extends only to informing and discussing with the attending physicians and to giving information about the proposed research programme, its objectives and protocols. This obligation does not require researchers to obtain the consent of the attending physicians.
- 6.42. The existence of attending physicians (or the likelihood of the existence of such attending physicians) should be disclosed to the IRB by the PI at the time that the research application is being made.
- 6.43. The IRB may then consider whether informing and discussing with the attending physicians should be made a formal requirement of ethics approval. Such a requirement should be made upon considerations that include, but are not limited to, the following:
  - (a) In the case of research that involves *any* level of clinical interaction with patients being treated or managed for medical conditions relevant to the proposed programme of research, researchers should be required to contact and inform the attending physicians. The IRB should decide on the facts of each case whether or not there is a sufficient connection between the proposed programme of research and the clinical treatment and management of the subject-patients, bearing in mind the interests of ensuring the safety, health, dignity, welfare and privacy of the subject-patients. Where the IRB is satisfied that there is no reasonable connection between the research programme and the treatment and management of the subject-patient, the researchers may dispense with informing and discussing with the attending physicians of their subjects;
  - (b) In the case of research that involves access to patients' medical records but with minimal levels of clinical interaction (e.g. the taking of blood or urine samples) or only social interaction (e.g. interviewing the subject-patient for a history), the IRB may in its discretion make formal contact and discussion a condition of ethics approval if it takes the view that the proposed interaction is relevant to the continued medical treatment and management of the subject-patient. Otherwise, researchers may in such cases dispense with contacting the attending physicians; and
  - (c) In the case of research that involves access to and a study of patients' medical records without any kind of contact between researchers and the patients, researchers need not inform or discuss with the

attending physicians (on the assumption, of course, that they have complied with all other applicable requirements).

- 6.44. In no circumstances should any researcher alter or modify in any way (whether in formulation, dosage or timing) any drug or other clinical regimen prescribed by the attending physicians of the subjects without first seeking and obtaining the approval of both the attending physicians *and* the IRB.

## SECTION VII: INSTITUTIONS

### 7. Institutions

#### The Responsibilities of Appointing Institutions

- 7.1. Institutions have the overall responsibility of ensuring the proper conduct of Human Biomedical Research and the protection of human subjects in all Human Biomedical Research carried out on their premises or facilities, or by their employees, or on their patients, or involving access to or use of human tissue collections in their custody, or involving access to or use of medical records or other personal information in their custody.
- 7.2. Every institution involved in Human Biomedical Research as defined in these Guidelines should establish and maintain an effective IRB. The IRB is accountable to the appointing institution, which must accept legal responsibility for the decisions of its IRB.
- 7.3. Institutions should lay policies for the composition of IRBs and the formal appointment of IRB members in accordance with the general principles and guidance presented in these Guidelines and, in particular, those set out under “Specific Operating Procedures for Institutional Review Boards” in Section V.
- 7.4. It is the responsibility of institutions to provide adequate resources and administrative support so as to enable IRBs to discharge their duties and responsibilities in an effective and timely manner.
- 7.5. Workload. Institutions should ensure that IRBs are not given a workload that compromises the quality of their work and IRBs should likewise ensure that their workload does not compromise the quality of their review. If this is likely, the institution is obliged to establish additional IRBs, to enlarge the membership of the IRB or to make formal arrangements for other IRBs to provide an opinion.
- 7.6. Institutions are obliged to ensure that IRBs receive adequate administrative support that is commensurate with the central role of the IRB in the ethics governance process. In this respect, the institution may take steps to lighten the workload of IRBs by delegating review in specific areas to a subcommittee, or by delegating some of its administrative or supervisory tasks to a separate well-staffed administrative body.

- 7.7. Such full-time administrative support should be sufficient to allow the IRB to:
- (a) Ensure continuity and consistency in the work of the IRBs;
  - (b) Discharge any continuing review and supervisory obligations, outcome assessment and reporting duties;
  - (c) Ensure that the IRB's decisions are made with regard to previously established precedents and decisions that they and their predecessors have made; and
  - (d) Ensure that proposals are reviewed and dealt with in a timely manner within the target time frames set by the institution.
- 7.8. The core members of the IRB should be able to devote sufficient and protected time commensurate with the workload of the IRB.
- 7.9. Institutions are also responsible for providing their IRB members with a full indemnity as set out in paragraphs 7.17 to 7.22 and this should be reflected in their letters of appointment.
- 7.10. Institutions providing care should retain responsibility for the quality of all aspects of care afforded to human subjects whether or not some aspects of care are part of a research study.
- 7.11. Medical Records and Patient Information. We recognise that the issues arising from access to the use of and the custody of medical records and other patient information are becoming increasingly complex. In this area, the ethical issues are inextricably interwoven with legal considerations, and the impact of the existing law is currently unclear in many situations. We hope to explore these issues in a separate subsequent report.
- 7.12. In the context of institutions such as hospitals with centralised patient records and databases, we recommend that appointing institutions take steps to determine who within the administrative structure should be the proper administrative custodians responsible for patients' medical information in the institution, and to advise their IRBs accordingly.
- 7.13. In situations where any of the researchers are also the administrative custodian of patients' medical information within the institution, procedures should be established to address actual, potential or apparent conflicts of interest.

- 7.14. Institutions should ensure that clear formal procedures are laid down for the release of all kinds of patients' medical information, and should formulate these procedures in consultation with their IRBs.
- 7.15. It is desirable that the IRB be given authority by its appointing institution for the ethical clearance of access to patients' medical information for research within the institution, so that no patients' medical information may be released for research purposes without clearance by the IRB except for cases of Exempted Reviews referred to in paragraph 3.15.
- 7.16. Training and Education for IRB members. We recognise that training for IRB members can only be beneficial in the scheme of ethics governance of human research. We therefore recommend that institutions that conduct Human Biomedical Research and which are required in the context of these Guidelines to have IRBs, should also have in place programmes for the training and education of IRB members. Hospitals that have sizeable research programmes should in particular have such programmes. Such training and educational programmes should, where possible, also be provided to research staff.

### **The Protection of Institutional Review Boards**

- 7.17. Notwithstanding the important role played by IRBs in research institutions, IRBs sometimes experience difficulties in attracting members of their choice in that some of the most qualified potential candidates for membership decline the invitation to serve. These candidates may do so out of a fear of legal liability in the event of a contested decision, or a decision that has an unexpectedly adverse impact on human subjects. Few such candidates have any legal training and their reluctance on this ground is understandable.
- 7.18. On this point, we note that the NMEC Guidelines recommend that IRBs should look to the authority appointing them to give IRB members formal indemnity "against the cost of any legal representation and any compensation ultimately awarded to human subjects" (Section 3.34). The NMEC Guidelines further recommend that such an indemnity be given in IRB members' letters of appointment.
- 7.19. IRB members discharge an important office in the public interest in the protection of human subjects. Often they do so for minimal or token remuneration, or none at all. Their only motivation being a call to duty and their only reward being the satisfaction of a job well done.

- 7.20. We take the view that IRB members should be fully protected in the discharge of their duties, provided that they do so in good faith, against any liability arising from their actions. Appointing institutions should give IRB members a full indemnity and arrange for the necessary insurance.
- 7.21. Legal protection for IRB members acting in good faith would also encourage the best and most competent individuals (both within and outside the medical profession) to contribute their skill and expertise to the IRBs, and help ensure that members are selected from the best available experts in their fields.
- 7.22. Because IRBs act as their appointing institutions' officers and agents, institutions remain liable to human subjects from any claim in tort and should be required to take out appropriate insurance coverage against the variety of claims that may arise in the course of the work of the IRB (for example, in relation to the approval of multi-centre or multinational research).

## **SECTION VIII: ACCREDITATION**

### **8. Accreditation**

#### **The Accreditation of Institutional Review Boards**

- 8.1. The current regulatory regime governing the review and approval of pharmaceutical trials (which we described in Section II) provides for a system in which applications for pharmaceutical trials are first screened by IRBs at the local institutional level before being forwarded to a national regulatory agency (the HSA) for approval. This system has served us well and is well understood by all parties involved in the process. It should continue to apply in the case of pharmaceutical trials.
  - 8.2. In the case of Human Biomedical Research other than pharmaceutical trials there is currently no national agency or regulatory body fulfilling a function equivalent to that of the HSA. The exception is the MOH, but it only has jurisdiction over hospitals, private clinics and other institutions falling within its purview under the Private Hospitals and Medical Clinics Act.
  - 8.3. The MOH provides guidance from time to time for IRBs falling within its jurisdiction. For example, the MOH has directed all IRBs to adopt and apply the NMEC Guidelines. From time to time, other directions are issued. Some of these are on the advice of the NMEC.
  - 8.4. The role of the NMEC, however, is to advise the MOH on ethical issues arising in the practice of medicine. The NMEC does not advise IRBs directly and does not function as a higher level appeal or advisory body to IRBs.
  - 8.5. Apart from complying with the directives issued by the MOH (including the NMEC Guidelines), IRBs in institutions under its jurisdiction are free to adopt such procedures, formulate their own standard operating procedures and determine their constitution, operating principles and other administrative practices.
  - 8.6. We recommend that all IRBs be formally accredited by the MOH, which should be empowered to audit, to investigate complaints (including complaints from research subjects) and to appoint external auditors and investigators at the cost of the institution being audited as part of the accreditation check or as a matter of routine audit for compliance.
-