

RESEARCH INVOLVING HUMAN SUBJECTS

GUIDELINES FOR IRBS

EXECUTIVE SUMMARY

Principle

1. There is general agreement internationally that human biomedical research involving risk of harm to human subjects should be subject to independent ethics review.
2. This principle is reflected in international documents such as the Nuremberg Code of 1949, the Declaration of Helsinki of 1964 and the International Conference on Harmonisation's "Guideline for Good Clinical Practice" (ICH GCP Guideline) of 1996.

Pharmaceutical Trials

3. In Singapore, pharmaceutical trials are currently governed under the Medicines Act and the Medicines (Clinical Trials) Regulations. All proposals for pharmaceutical trials are required to undergo an independent ethics review process and to comply with the "Singapore Guideline for Good Clinical Practice" (SGGCP), which is based on the ICH GCP Guideline.
4. This independent review is carried out first at the institutional level by the institution's ethics committee or institutional review board (IRB). If approved, the proposal is then submitted to the Health Sciences Authority (HSA), which is the licensing body for pharmaceutical trials. Clinical Trial Certificates will be issued for proposals approved by the HSA.

Human Biomedical Research other than Pharmaceutical Trials

5. Currently, there is no provision requiring human biomedical research other than pharmaceutical trials to be submitted for independent ethics review. This is so even if the proposed research programme entails a risk to the health, safety or welfare of the human subject.
6. Since 1998, the Ministry of Health (MOH) has required all government and restructured hospitals to establish ethics committees or IRBs. Hospitals are required to comply with the “Ethical Guidelines on Research Involving Human Subjects” (NMEC Guidelines) issued by the National Medical Ethics Committee (NMEC) in 1997.
7. The NMEC requires all research protocols that involve human experimentation, whether pharmaceutical trials, trials of new medical devices, new procedures or any other forms of clinical studies that require the participation of human subjects or the use of human tissues or organs, to be submitted to ethics committees or IRBs for review.
8. Considerable changes have taken place since the NMEC issued its guidelines. Most significantly, the volume of human biomedical research other than pharmaceutical trials has increased sharply and now far exceeds that of pharmaceutical trials. There is also a much greater diversity in the kinds of human biomedical research being carried out in Singapore.

Objectives

9. In these Guidelines, we build on the work of the NMEC. Our primary objectives are:
 - (a) To review the current system of ethics governance of human biomedical research in Singapore, with particular focus on the processes and procedures;
 - (b) To advance recommendations and operational guidelines on the constitution and role of ethics committees or IRBs in the ethics governance of human biomedical research; and
 - (c) To provide guidance in Singapore for the promotion of ethically responsible human biomedical research conforming to the best international standards and practice.

10. These Guidelines aim to make clear the roles and responsibilities of IRBs, researchers and institutions in order to achieve objective and independent ethics review of research proposals involving human subjects.
11. In advancing these Guidelines, we also aim to foster a culture of good practice, transparency and accountability for IRBs and the adoption of sound standard operating procedures and other elements of good practice. In doing so, we also aim to encourage the best qualified persons to come forward to serve on the IRB of their institutions.
12. Finally, we hope that in establishing clear and transparent rules, standards and procedures, the reputation of Singapore as a global centre of excellence in biomedical research will be upheld and strengthened.

Does All Biomedical Research Involving Human Subjects Require Ethics Review?

13. In our view, not all biomedical research involving human subjects needs to undergo the full formal process of ethics review. Human biomedical research is of fundamental importance to the advancement of biomedical knowledge, and hence to the public good. A balance, therefore, has to be drawn between the imperatives of advancing and encouraging human biomedical research in the public interest and the need to protect the health, safety, dignity, welfare and privacy of human subjects.
14. It is generally and internationally accepted that some categories of human biomedical research may be either exempted from ethics review (Exempted Review) or may undergo a less formal fast-track ethics review process (Expedited Review) if there is no risk or minimum risk to the human subjects. The adoption of these two categories is consistent with the current practice in the biomedical research and medical communities of leading scientific jurisdictions around the world.
15. In Section III, we review and offer guidelines on the kinds of human biomedical research that ought to be subject to ethics review and on the categories of such research that could be considered for Exempted Review and Expedited Review.
16. We make a distinction between Direct Human Biomedical Research, which involves direct interference or interaction with the physical body of a human subject, and Indirect Human Biomedical Research, which does not involve such direct interference or interaction (for example, populational studies involving only the examination of medical information with no contact or interaction with human subjects). As risks of harm to the health, safety and

welfare are likely to be much less and much more remote in Indirect Human Biomedical Research, we suggest that research proposals of this class could be considered for Exempted Review or Expedited Review.

Applicable Principles

17. In Section IV, we expand on the principles laid down by the NMEC in the NMEC Guidelines and generally on the ethical principles to be applied by IRBs in the ethics review of research proposals.
18. The fundamental objective of having a system of ethics governance for research involving human subjects is the protection of the safety, health, dignity, welfare and privacy of these subjects.

Summary of Main Recommendations:

General

19. All Human Biomedical Research should be reviewed and approved by a properly constituted IRB before it is allowed to proceed. Some research, however, could qualify for Exempted Review or Expedited Review if it involves no risk or minimal risk to the safety, health, dignity and welfare of the research subjects and provided that the protection of the subjects' privacy is strictly observed.
20. It is recommended that all IRBs be formally accredited by the MOH.
21. These Guidelines apply to all Human Biomedical Research wherever such research may be carried out in Singapore, whether or not such research is carried out in an institution under the direct jurisdiction of the MOH pursuant to the Private Hospitals and Medical Clinics Act.

IRBs

22. IRBs are accountable to their appointing institutions and they are responsible for:
 - (a) The ethics review and approval of proposed Human Biomedical Research programmes;
 - (b) The continuing review and supervision of the research programmes approved by them;

- (c) Reporting to their respective institutions any unusual or unexpected events arising from the research;
 - (d) Providing feedback to and maintaining dialogue about applicable standards with their constituent researchers; and
 - (e) Receiving feedback from research subjects.
23. In the ethics review process, IRBs must be aware of any actual, potential or apparent conflict of interest and take reasonable steps to avoid or minimise such conflicts.
24. The scientific review of research proposals does not lie with the IRB. It is for the researchers to satisfy the IRB that an objective review of scientific merit has been carried out and to make these findings (whether positive or negative) available to the IRB.
25. In 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. The local portion of a multinational research programme should be subject to review by the local IRB.

Researchers

26. Researchers must comply with all the conditions laid down by the IRB that approved their project.
27. Researchers are also responsible for ensuring that their research complies with all relevant laws and other regulatory obligations and requirements.
28. Researchers are required to inform and seek approval from their IRBs for any proposed variations from the terms of approval of the projects before such variations can be implemented.
29. Researchers should submit annual (or more frequent) progress reports as required by their IRBs, as well as project completion reports and reports of adverse events.
30. Researchers should inform and discuss with the research subjects’ attending physicians if the research involves interfering with the subjects’ medical management.

Institutions

31. Institutions have the overall responsibility of ensuring the proper conduct of Human Biomedical Research carried out by their employees on their premises.
 32. Every institution involved in Human Biomedical Research as defined in these Guidelines should establish and maintain an effective IRB. The institution must accept legal responsibility for the decisions of its IRB. IRBs may be shared by more than one institution. They could also be domain specific, providing more focused and specialised ethics review.
 33. Each institution must set up clear policies for the establishment and operation of its IRB. The institution will determine the composition and constitution of the IRB, the specific operating procedures for ethics review and categories of research for Exempted Review and Expedited Review.
 34. Institutions are responsible for providing their IRB members with full indemnity.
 35. Institutions, in particular those with sizeable research programmes, should have in place programmes for the training and education of their IRB members.
 36. Institutions should, in consultation with their IRBs, ensure that clear formal procedures are laid down for the release of all kinds of patients' medical information.
 37. Institutions should also ensure that there are adequate resources to enable their IRBs to discharge their duties and responsibilities in an effective and timely manner.
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