DIALOGUE SESSION ON THE CONSULTATION PAPER "ADVANCING THE FRAMEWORK OF ETHICS GOVERNANCE FOR HUMAN RESEARCH"

20 Chairpersons and Representatives of the hospital ethics committees or institutional review boards (IRBs) of 17 organisations met with seven members of the Bioethics Advisory Committee (BAC) on 7 November 2003. This Annexe provides a summary of the comments and concerns raised at the dialogue session between the parties.

Organisation Represented:

1. Alexandra Hospital
2. Changi General Hospital
3. Health Promotion Board
4. Institute of Mental Health/Woodbridge Hospital
5. Institute of Molecular and Cell Biology
6. KK Women's and Children's Hospital
7. National Cancer Centre
8. National Dental Centre
9. National Healthcare Group
10. National Heart Centre
11. National Medical Ethics Committee
12. National Neuroscience Institute
13. National University Hospital
14. National University of Singapore
15. Parkway Group Healthcare Pte Ltd
16. Singapore Tissue Network
17. Tan Tock Seng Hospital

Summary of Comments and Concerns Raised at the Dialogue Session

Intention of the Consultation Paper

IRB: Rules set for the industry quickly become obsolete given the speed of progression in biomedical sciences.

BAC: The preliminary Recommendations advanced in the Consultation Paper (Paper) are not meant to be cast in iron but will be reviewed as and when the need arises. This is to be expected not only with the advancement of science, but also as values and laws of the society evolve over time. The intention behind the Paper is to establish a framework for the Government to consider when to implement appropriate policies on the ethics governance of human research. One of the main motivations of the Recommendations is to harmonise the ethical standards for all research institutions and their IRBs. Such standards, as prescribed in the Paper, are universally accepted and hence would provide greater public assurance.

Role of Principal Investigators

IRB: In large multinational studies, a local principal investigator (PI) should have a greater role in the design, conduct, monitoring and analyses of the studies.

BAC: This concern is noted and will be highlighted to the Ministry of Health (MOH).

Requirements in Obtaining Informed Consent

IRB: One of the provisions in the Paper is for a witness to be present at the consent-taking process (paragraph 5.57). Will the witness be required to observe the entire process or just the endorsement of the consent form?

BAC: The purpose of that provision is to have an independent person ensure that the human subject understands what he/she is consenting to. This requirement does not entail any departure from normal medical procedures. As the Paper is meant to provide only a framework for ethics governance, the actual procedure for the procurement of consent will not be prescribed here.

Role of a Supervisory Body for IRBs

IRB: Will there be a central body to keep check on the standards of ethics governance of each institution? If so, some form of penalty needs to be prescribed for non-compliance so that the standards can be effectively maintained. Revocation of the accreditation of an IRB can be such a penalty.

BAC: The BAC recommends that a central supervisory authority be established to either license each institution or grant an umbrella licence to a group of institutions. This authority will be empowered to accredit and audit licensed institutions. A majority of the large hospitals will be licensed by their areas of competence. Licence can also be granted based on specific conditions. Such a

supervisory authority will therefore impose two kinds of checks – licensing and accreditation.

Role and Responsibilities of IRBs

Continuing Review, Supervision and Audit

IRB: Can the BAC clarify what it means by "continuing review" (paragraph 5.15.2)?

BAC: The BAC has received several responses on this issue. By "continuing review", the BAC intends to empower IRBs to carry out audits. This empowerment will change the mindset of some PIs who consider the IRB approval of research proposals as a one-off threshold clearance. IRBs should review on-going research even after it has given its initial approval for the research proposal. The Paper will be amended to clarify this issue.

IRB: Can a separate body be assigned to conduct audit in order to alleviate the workload of IRBs?

BAC: An IRB need not perform the audit itself but it has to have the means to monitor any deviations from the proposed research protocol. For example, the IRB can mandate an annual report and a completion report, or it can appoint independent auditors to carry out audits.

However, it may be better for IRBs to carry out audits themselves, as appointing independent auditors may result in IRBs having to check on two parties. A research may have wide social impact and IRBs should ensure that the research is done in accordance with the approved protocol, with particular focus on the safety and privacy of human subjects. Other concerns, such as scientific validity of the research, are secondary.

IRB: This is not feasible. Some IRBs are currently overloaded with protocols for review (200-400 per year). It is not only difficult for IRBs to find time for the added audit responsibilities, but is also difficult for IRBs to find people with the time and capability to perform independent audits on their behalf. In addition, certain IRBs have difficulty coping with a large number of annual reports.

BAC: Institutions should provide their IRBs with adequate resources to enable them to discharge their responsibilities.

In addition, institutions should be the ones to select the independent auditors. The main requirement of audit is to assess ethical merits, not scientific merits.

IRB: Although not officially or legally empowered, one impression is that IRBs have the power to investigate ethics violations even after the protocol has been approved. Do the recommendations require more of IRB than what is already being done?

BAC: IRBs will need to report to a national supervisory body.

IRB: The Singapore Guideline for Good Clinical Practice (SGGCP) has clearly delineated the roles of monitors, sponsors and auditors. The Paper should follow the SGGCP's framework so that the IRB's responsibility is clearly and primarily confined to a review of documents.

BAC: One of the purposes of this Paper is to extend the rules in the SGCCP on clinical drug trials to non-drug trials. An IRB is not the enforcer of these rules and these provisions should not lead to unnecessary bureaucracy that stifles research.

IRB: There are situations where IRB members find it difficult to confront researchers who are very senior in rank. In fact, many researchers in certain countries who have flouted ethics rules were highly regarded PIs.

There is a huge gap between the recommended standards and what IRBs can achieve. While the responsibilities spelt out are probably appropriate, IRBs currently do not have the capacity to take on all of them.

BAC: In the UK, IRBs are not the ones who conduct investigation at the research level. It is important for IRBs to have the power to require that an audit be performed. Such controls will reassure the public that adequate protection is in place.

IRB: The responsibilities of IRBs in reviewing, supervising and auditing, as well as the means of discharging these responsibilities, need to be more clearly defined. Often, the problem lies not with the lack of regulations (because these are present), but with the lack of people to implement them. Monitoring and auditing of research protocols should be conducted at two levels: at the institution-level, at which independent inspectors are authorised to examine any records at random and report their findings to the IRB; and at the level of the accreditation body, which can mandate that research institutions submit reports.

However, the two-tier approach will be cumbersome. Instead, IRBs should be allowed to decide which projects will require continuing review. It is likely that the IRBs will be asked by their institutions to recommend suitable candidates for the role of auditors, but IRBs may not be able to do so. Therefore recommendations from the BAC or the national supervisory body will be desirable.

BAC: It is the PIs' responsibility to report changes in the protocol to their IRBs and should not require the IRBs to press them to do so. The BAC will make clear recommendations for necessary resources to be made available by institutions and for reports to be made available to the IRBs. The BAC will attempt to do this without introducing excessive bureaucracy to the system. Reports are required for internal audits of most institutions. Hence the requirement for reports to be submitted to the IRBs should be no more than a small responsibility. The kind of audit which the BAC has in mind should be simple

and manageable at a certain level by non-medical staff. More important, institutions should ensure that IRBs have sufficient time to perform their functions. IRBs should grow beyond honorary bodies to become full administrative bodies. There is also a need for institutions to provide legal protection for IRB members.

Responsibility for Scientific Review

IRB: IRBs are often required to assess scientific merits besides ethical merits. Most institutions do not have enough resources to support both an ethics review board and a scientific review board.

BAC: The BAC understands that a proper ethics review should take into account scientific merits, but the BAC's focus is on the social impact of the research. The BAC recognises that small institutions may not be able to set up a separate scientific review body. Hence it allows institutions the freedom to decide if they want their IRBs to be responsible for both ethics and scientific review.

Requirement for IRB Members to Meet Face to Face

IRB: Other forms of meeting such as by teleconference or video-conference should be acceptable forms of meetings besides a face-to-face meeting. Such forms of meetings were used by institutions during the SARS crisis.

BAC: These other forms of meetings are acceptable. The intention of requiring face-to-face meetings is to ensure proper communication and decision-making. Decisions should not be made by way of e-mail correspondence. The BAC is concerned that an IRB member may not be fully aware of another member's evaluation of, and comments on, a research proposal under review.

IRB: There are international requirements, such as in the US, for IRB members to meet face to face. Singapore should conform to such international practices.

BAC: Certain research proposals may be subject to expedited review and thus a decision need not be made at a face-to-face meeting.

Special IRBs

IRB: In some countries, IRBs are removed from the auspices of institutions and yet some other institutions, such as the UK National Health Services, share IRBs. The motive is to secure the independence of IRBs from their appointing institutions and thereby avoid conflict of interest.

However, it is the institution's responsibility to ensure that its appointment of IRB members will not result in any conflict of interest. If an IRB is separated from an institution, it will not be able to familiarise itself with the operations of that institution. Hence, the two-tier approach is a good one.

However, there are commercial IRBs in the US that are independent of an institution. These IRBs have been mentioned in the Paper. They can be an option for us. The members of commercial IRBs are recruited from a large range of institutions. They do not serve on the IRB full-time and are paid about US$200 per protocol reviewed.

BAC: A reason for the acceptance of commercial IRBs in the US is that they provide a liability shield for research institutions, as these IRBs are adequately insured. The concept of commercial IRBs is culturally new to Singapore and may not be applicable within the local context.

In a small nation like Singapore, IRBs operating outside an institution will not solve issues of conflict of interest. Nonetheless, the BAC welcomes the idea of shared IRBs or domain-specific IRBs, which have been described in the Paper.

IRB: Domain-specificity is advantageous as there will be a need for IRB members with the suitable expertise for evaluating specialty research protocols. Another potential problem to note with respect to the small size of the local medical community is the 'rubber-stamping' of one another's research protocol, because most of members of the community recognise one another's field of work.

Conclusion

BAC: The BAC will consider all suggestions that have been made and will try to address as many of the issues that have been raised. Some of the provisions in the Paper may have been misinterpreted as excessive. These provisions will be clarified by the BAC in its recommendations to the Government. It is emphasised that the provisions and recommendations issued by the BAC are only intended as general guidelines. The BAC thanks all participants for their time and valuable input.