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University of Zimbabwe

Making research ethics review work in Zimbabwe — the case for investment in local capacity

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Abstract

Objective: To describe the status of ethics review as pertaining to medical research in Zimbabwe, to compare this with international guidelines, and thus to identify potential improvements in the process.
Design: The description includes background about the national review body, the Medical Research Council of Zimbabwe (MRCZ), and the findings of an analysis of institutional ethics review performed by the MRCZ liaison office.
Results: Discrepancies with international guidelines include application of the concepts of independent and competent review, monitoring of ongoing studies, and ensuring appropriate membership of institutional ethics review committees (IRECs).
Conclusion: A focus on research ethics education for researchers and IREC members, as well as ensuring appropriate respect for IREC review, are opportunities for improvement in the process.

Cent Afr J Med 2004;50(11/12):115-19

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Introduction

Much has been written in recent years about the need to improve research ethics review in developing countries. Because of the involvement of researchers and sponsors from North America and Europe, including pharmaceutical companies, in clinical trials involving human subjects in developing countries, concerns about exploitation and ethical imperialism (imposing the standards of another country on research performed) have been raised. International guidelines have been revised, and new ones developed, with greater emphasis on local expertise, relevance and policies. In some countries, significant levels of sophistication in terms of the protection of research participants are demonstrated, for example India has published "Ethical guidelines for biomedical research on human subjects".

However, the operational groups (institutional research ethics committees [IRECs], also called research ethics boards and institutional review boards) which are relied upon so heavily everywhere to implement guidelines, policies and rules, are critically under-equipped for this task in many developing countries, virtually guaranteeing failure of human subject protection.

This paper describes and analyses the situation in Zimbabwe, a typical sub-Saharan country, in an effort to plan effective improvements in research ethics review in a developing country.

Background.

In 1974, the then Rhodesian government set up the Medical Research Council, now called the Medical Research Council of Zimbabwe (MRCZ), by an act of parliament.[1,2] (This was shortly after the US created its national Commission for the Protection of Human Subjects of Biomedical and Behavioural Research.) The MRCZ is semi-autonomous and has 14 members representing different stakeholders such as the Zimbabwe Medical Association (ZIMA), Life Offices Association, Universities, and National Association of Medical Aid Societies. The chairperson is nominated by the Minister of Health. The council has a mandate to regulate research by review, approval and monitoring, but has limited legal powers. At the present time it reviews about 150 proposals a year, of which about 30 are from outside the country. (However, many proposals are NOT reviewed by the MRCZ, due to inadequate enforcement of regulations). Some policy directives and guidelines have been issued from time to time, such as the "*Guidelines on the collection of blood samples for research purposes.*" The emphasis has been on building a relationship of trust between all the stakeholders involved in research with the MRCZ playing a facilitatory role. Some efforts toward revising the appropriate piece of legislation have been initiated recently, attempting to give the MRCZ authority to deal with non-conforming researchers. One major problem in trying to drive towards a regulatory system has been the limited capacity of the MRCZ in terms of financial and human resources necessary.

Another body charged with reviewing medical research is the Medicines Control Authority of Zimbabwe, which has regulatory powers over clinical trials involving the testing of medical drugs and devices.

After a workshop hosted by the MRCZ in 1994, Institutional Ethical Review Boards (IERBs, here called IRECs) were set up in major institutions. The intention was that research proposals would be reviewed at the researchers' home institution first, and passed on to the MRCZ with recommendations, for final review and approval. Proposals from foreign investigators, including pharmaceutical companies, would go from IRECs to the Research Council of Zimbabwe before they are submitted to the MRCZ or to both the MRCZ and or MCAZ. In the subsequent sections some of the problems encountered with these IRECs will be discussed.

Formation of IRECs.

These were first formed in 1995 after a workshop on Ethical Issues in Reproductive Health Research hosted by MRCZ and sponsored by WHO-AFRO, in response to the increasing number of HIV/AIDS studies and the ethical issues that relate to such studies e.g. confidentiality.[3]

Difficulties for the IRECs.

Recent analysis of ethics review by the MRCZ liaison office revealed a number of problems for IRECs from the perspective of local bodies:

1. Little was done in the way of providing written or other guidelines and support on how the IRECs were to function.
2. There was little communication or other follow up between IRECs and MRCZ.
3. Consequently, the review procedures and their quality have not been standardised
4. Without adequate guidelines and standardisation, review procedures have been incomplete and inadequate.
5. At the time of IREC formation, and subsequently, there has been no training for IREC members and reviewers.
6. Many reviewers have no background to equip them specifically for research ethics review, and would be more comfortable with purely scientific review.
7. After six years, some IRECs are no longer functioning, with some operating nominally only, or as one man committees. This is probably a symptom of a number of other problems.
8. IREC membership is voluntary, unpaid and not recognized as legitimate professional activity by management in the tertiary institutions. Thus participation in IREC work, despite being arduous and time-consuming, is time spent away from "real" work, which may place members at academic or financial disadvantage. Although these complaints are not unique to the developing world, they are more pressing, given the large range of responsibilities with which health professionals there are routinely burdened in their circumstances of staffing shortages.

With poor motivational factors of this nature, it is hardly surprising that nonattendance and drop-out rates from IREC meetings are unworkably high.

9. Ethics education and awareness among researchers is not at a high level, ethics review is regarded as a nuisance, and many investigators do not submit their proposals to IRECs for review if possible. When a "sign-off" from a local ethics research board is required for overseas funding agencies, the single surviving member of the IREC (usually the chairperson, frequently also the administrative head of the institution) provides a convenient signature. Thus much more ethics education at the level of training for investigators (medical school undergraduate and post graduate courses) is needed if researchers are to be motivated to submit their research proposals to research ethics review boards willingly.
10. Without effective monitoring of research, the IRECs have no "teeth". As there are already many constraints to designing and carrying out research in seriously resource-limited environments, researchers will often cut corners where they can, realizing that this will improve the likelihood of being able to carry out the project. Paradoxically, stringent review requirements may prevent many worthwhile research efforts. If research was simply not permitted without ethics clearance, all studies would be submitted. Monitoring is expensive, however, and dedicated staff would be required.
11. Limited support from government, in the way of financial and administrative assistance, has two results. Firstly, it suggests to the IRECs that they are of no great importance to the Ministry of Health, so that they should not take their task too seriously. Secondly, the many aspects involved in the logistics of running meetings effectively (contacting members in time, distributing minutes and proposals, executing decisions, contacting investigators, gathering information, arranging educational activities, etc.) are performed much less well without dedicated, employed staff.
12. The quantity of research in some developing country institutions may not be as much as in similarly-sized facilities in North America or Europe. Consequently a separate IREC, with all the commitment that entails, may be both unnecessary and difficult to sustain for each institution. On the other hand, the more removed a committee is from the site of the research, the less likely it is to adequately consider local factors.

How should IRECs function?

In this section, guidelines for the functioning of IRECs are described. These have been effectively formulated by experts, and are here paraphrased from the "*Operational guidelines for Ethics Committees that review Biomedical Research*" that were developed by the World Health Organization.[4] On the basis of these guidelines suggestions for the resolution of the difficulties described in the previous section will be attempted.

1) **Purpose** — IRECs exist to protect subjects of medical research, in the case of human participants by guarding respect for persons, and by ensuring that the benefits and burdens of medical research are distributed justly. They do this through –
   a) Independent and competent review of the ethics of proposed studies.
   b) Ensuring regular monitoring of ongoing studies.
   c) Making decisions in the interest of potential research subjects as well as their communities.
2) **Membership** — IRECs require members:
   a) From different disciplines and sectors, thus reflecting balanced age, gender and in multicultural societies cultural/ethnic composition;
   b) Who are laypersons, preferably from the communities which are proposed to be studied;
   c) With understanding of the scientific aspects of the proposals;
   d) Without conflict of interest.

   IRECs consist of some members who fall into category (b), others who are (c). All will benefit from ongoing education in research ethics.
3) **Review** — this should consist of a critical analysis of:
   a) Scientific design and methodology (validity, harm-benefit analysis, justification for controls, stopping rules, monitoring procedures, publication plans);
   b) Research subjects recruitment (study and sample populations and demographics, recruitment procedures, inclusion and exclusion criteria);
   c) Research subjects protection (investigator competence, justification for any withdrawal or withholding of standard therapy, health care for research subjects, arrangements for ongoing access to the study product after the study, compensation and costs to subjects);
   d) Confidentiality for subjects (who will have access to personal data, and how will this information be kept private);
   e) Informed consent process (adequacy of the informing process, clear justification for inclusion of individuals who cannot give consent);
   f) Community considerations (local relevance, impact, consultations, influence of community on individual consent, local health care development).
4) **Decisions** — should only be reached:
   a) By a quorum of members who have reviewed the application;
   b) After sufficient time for discussion has been permitted;
   c) By members without a confliet of interest (if such a conflict is present, the affected member

should be excused from the room for that review);

d) Through consensus if possible (if not, by a previously defined voting arrangement);

e) With clearly stated written reasons which will be communicated to investigators, including suggestions for revision.

Opportunities for improvements.

Comparing the ideals immediately above, and the realities of Zimbabwe, what can be done to enhance the process?

a) "Independent and competent review of the ethics of proposed studies."

Independence can only be achieved by ensuring that no undue influence on decisions is exerted by other individuals and bodies, such as the parent institution, government ministries etc. A formal enshrining of the independence of the IREC in a charter or constitution may help, but only partially. The expectations of influential investigators bringing international drug trials with the promise of great national benefit to the IREC of a developing country hospital, for example, may be very difficult to resist. Effective solutions can only be sought in a long-term effort to inculcate ethics concerns into the mind-set of all researchers. In other words, research ethics needs to be a part of the training (and continuing medical education) of all medical researchers.

Competence is critical, and entails having adequately trained individuals performing the task assiduously and scrupulously. There are many stumbling blocks to be overcome (see points five and six of difficulties for the IRECs above). With a much smaller pool from which to draw suitable IREC members, many developing countries' institutions end up with committees composed of ill-suited individuals. Poor recognition of IREC work, and overcommittment of health professionals (including personal affairs, e.g. private practice, because of poor remuneration), are sure predictors of irregular and unenthusiastic participation. To overcome these, IREC membership could be associated with academic prestige (e.g. promotion prospects), financial incentive, and strict criteria, so that it becomes a matter of pride to be invited to join such a group. Since few eligible candidates may exist in a single institution, one IREC could be formed for a number of institutions, for example a single IREC for all research in Harare. This would also be commensurate with the likelihood of fewer applications in a single institution than in a comparably sized one in the developed world. (See 12. above), but does introduce the difficulty of needing to make sure that the IREC reviewers are familiar with each institution's details as they relate to a research environment, even if they are not connected to that institute (for example research emanating from a psychiatric hospital has ethical problems which may be unfamiliar to reviewers not connected with such a hospital).

b) Ensuring regular monitoring of ongoing studies.

Monitoring of studies is difficult, not only in developing countries. Many large projects have their own data safety monitoring boards, designed to be independently critical, and a regular report from such a board to the IREC on the progress of a study could fulfill this requirement. It must be remembered that the data safety monitoring board is not primarily concerned with all ethical aspects of the study, however, and may not be as scrupulous, for example, in reporting changes in community perceptions and desires regarding a drug trial, as it might be about adverse drug events. Nevertheless, a truly independent monitoring system for all research may simply not be feasible for many developing countries, and the co-operation and compliance of investigators will need to be relied on in any attempts to monitor ongoing work. The establishment of independent monitoring units risks outrage by public health officials perceiving unwarranted expenditure of precious public funds. Requirements for the annual renewal of licensing of a project, with submission of interim results, would assist the process without much financial burden.

c) Ensuring appropriate membership of the IREC.

In addition to the points in (a) above, improving knowledge of current IREC members can significantly change the way decisions are reached. Providing training, in the form of short courses (one to three days), reading material, and short presentations by visiting experts at IREC meetings, may strike the balance between the need to impart information, and the limited time available to IREC members for educational activities. This is an important area for international agencies to contribute to in terms of experience and funding — for example a two week course for 50 IREC members from Africa and Asia held by the NIH or the Nuffield Foundation, with the contributions of experts from developed and developing countries, would begin to address many difficulties experienced by those reviewers. Sponsorship for participation in the Global Health Forum for Research Ethics could lead to the formation of networks and linkages between reviewers and bioethicists.

One difficult issue concerns the presence of eminent personalities. Respected individuals can exert disproportionately effective influence by virtue of their standing in the institutional community, and cause skewed decision-making. The solutions are to either re-train such an individual to permit other opinions to be included, or to persuade him or her to stand down from the IREC. Neither option is easy to carry out. It can be seen that the chairperson of the IREC plays a vital role, and should ideally be a respected and capable individual capable of motivating his or her committee to enact what may be quite radical changes. There is, therefore, an argument to be made in favour of efforts to increase capacity especially by concentrating on IREC chairpersons.

d) "Reviews should consist of....."

Since clear guidelines for IREC reviews are now available, these should be appropriated (altered where deemed necessary), discussed and debated at training sessions, made available in a permanent form to each IREC member (for example a laminated sheet), and adhered to by the

chairperson when conducting meetings. As in a number of other improvements, the problem of financial and other administrative support becomes important and merits being drawn to the attention of relevant policy-makers.

e) "Decisions should only be reached . . . by members without a conflict of interest."

Once again, the small numbers of eligible reviewers may render the suggested process difficult to follow. In addition, many reviewers are not aware of more subtle conflicts — they could be influenced by the prospect of more international recognition of a participating institution, the arrival locally of world renowned experts, and other indirect benefits. Lastly, the unfortunate possibility of IREC members becoming corrupted (bribed) should also be guarded against.

Conclusion

Recommendations for action in Zimbabwe.

1. Formally enshrine the independence of all IRECs in a charter or constitution.
2. Ensure appropriate IREC membership by associating with academic prestige (e.g. promotion prospects), financial incentive, and strict criteria, so that it becomes a matter of pride to be invited to join such a group.
3. Require a data safety board of larger studies, and at minimum annual renewal of licensing of all projects.
4. Provide training to improve knowledge of current IREC members, in forms appropriate to them, (an important area for international agencies to contribute in terms of experience and funding), and especially for chairpersons of IRECs.
5. Make easily accessible forms of IRECs review guidelines available to all members.
6. Form one IREC to function for a number of institutions.

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