Introduction by Susan Bull, November 2002

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Recent years have seen growing international debate about the ethics of conducting medical research in developing countries. Although many of the issues at stake do not differ in kind from those in more developed countries, the limited resources available within developing countries may exacerbate the problems faced. In addition, imbalances in power between the stakeholders in research — which can include multinational pharmaceutical companies, publicly funded researchers, national governments, and participants — can increase the risk of exploitation of the more vulnerable parties.

Aspects of research that have proved particularly controversial in developing countries include the relevance of the research to participants, standards of care provided to participants, the design and conduct of processes used to obtain the consent of research participants, the appropriateness of international and national guidance on research ethics, and the care provided to both research participants and the wider community once research is over.

Perhaps the most contentious issue at present is the standard of care that should be provided to participants in the control group of clinical trials. This was thrown under the international spotlight in 1997, when US-funded research into the prevention of mother-to-child transmission of HIV in Thailand was criticised in The New England Journal of Medicine and The Lancet. Participants in the control group were given a placebo, rather than a long course of antiretroviral treatment (which had been demonstrated to be effective in developed countries but was not routinely available locally).

The critics argued that, to prevent the exploitation of those in control groups, all participants should be provided with the best available treatment anywhere in the world, regardless of where the research is conducted. However, other researchers and research funders have argued that it is not always possible, affordable, nor appropriate, to supply a 'universal' standard of care in developing countries, and that the difficulties of meeting such a requirement would prevent beneficial medical research from being conducted.

Other discussions about the ethics of research in developing countries focus on the application of specific principles, including the need to respect the dignity of individuals (including respecting their autonomy), the need to remain sensitive to cultural differences, the need to alleviate suffering, and justice (including the need for fair distribution of the benefits and burdens of research).

There is widespread agreement that these fundamental ethical principles must underlie all medical research. Controversy arises, however, when decisions are made about applying these principles in specific circumstances, and when attempts are made to resolve conflicts that develop during their application. For example, the need to respect individuals — which requires that participants must consent to participate in research — can conflict with the need to remain sensitive to the local culture, in which it may be accepted that some adults (often women) do not make their own decisions about such matters.

One question that is receiving an increasing amount of attention — particularly within the context of access to antiretroviral treatments for HIV/AIDS — is what should happen once a research project in a developing country is completed. Concerns include:

- Ensuring that researchers receive appropriate recognition of, and where appropriate a share of the financial rewards for, their endeavours;
- How to sustain improvements to healthcare systems made during research; and
- How participants in research and members of the wider community can gain access to the benefits of research, in particular treatments demonstrated to be successful.

A related issue is the need for research to be relevant to the population in which it is conducted. At present, many developing countries have a limited capacity to determine national health and research priorities, or to conduct relevant research. As a result, they can become dependent on the interests of external sponsors. In such circumstances developing countries may find it difficult to refuse offers to sponsor research, even if it is unlikely to benefit their populations, because of the accompanying incentives, such as improved healthcare facilities and training.

Debates about ethics in medical research take place against a backdrop of international guidelines that have primarily been drafted in response to the way that medical research is conducted in developed countries and, in places, may therefore be of limited relevance to developing countries.

The cornerstone of much of this guidance is the World Medical Association's Declaration of Helsinki, first published in 1964. In the most recent revision, published in October 2000, the provisions about standards of care (section 29) and what happens after research is over (section 30) have been criticised as unattainable and inappropriate for developing countries.

More detailed guidance on the ethical conduct of medical research, drafted by the Council of International Organisations of Medical Sciences (CIOMS) was revised in August 2002. During the drafting process it became clear that once again the issue of the standard of care that should be provided to research participants was proving particularly difficult to resolve.

A few developing countries, including India, Uganda and South Africa, have formulated their own national ethical statements, which provide an intermediate step between the principles set out in international guidance and decisions about how these should be applied on a country-by-country basis. However, national and international guidelines cannot be effective unless countries have appropriate mechanisms for their implementation.

For example, an essential safeguard for research participants is an effective ethical review process for proposed research. A number of international programmes to support the establishment and development of ethical review committees in developing countries are in place. In many developing countries, however, review systems are unfortunately at a relatively early stage of development, and are sometimes of limited effectiveness. Particular care is needed when determining how research ethics committees can be

adequately trained and resourced, while remaining independent of governments, institutions and research sponsors.

This dossier addresses some of the key issues that face those engaged in funding, designing, reviewing and conducting medical research in developing countries. These include ethical aspects of the design of research and consent processes, what should happen once research is over, the development of local capacity to design and conduct research and systems for the ethical review of research, and an overview of current guidance and regulation. Links to relevant news items, organisations, regulations, reports and educational resources are also provided. We will provide regular updates about developments in this important area, and hope that the information provided will help to inform ongoing discussions and initiatives.

Susan Bull, November 2002
Ethics of research dossier coordinator