International research ethics guidelines under threat

A full-scale attack on the CIOMS Guidelines and the Declaration of Helsinki is currently underway.

Udo Schuklenk

During the Third Reich, Nazi doctors in German concentration camps conducted some of the most gruesome medical experiments imaginable. The international community responded to these and other crimes committed by medical researchers against research subjects, with the Nuremberg Code, the first international normative framework regulating the standards of clinical trials (1). This document was superseded in 1964 by the Declaration of Helsinki (2), a code for research and experimentation issued by the World Medical Association (WMA), which despite its partial dilution of the stringent ethics requirements set by the Nuremberg Code eventually became the most influential international ethics document regulating medical research. In 1993 the Declaration was supplemented by international research ethics guidelines produced by the Council of International Organisations of Medical Sciences (CIOMS) in collaboration with the World Health Organisation (3). This set of documents provides essential protection to research subjects in developing countries.

A full-scale attack on the CIOMS Guidelines and the Declaration of Helsinki is currently underway. Much of this article will deal with the Declaration of Helsinki. The reason for this is to do with the fact that the CIOMS deliberations take place in complete secrecy. The proponents of changes to the CIOMS research ethics guidelines are the same as those who push for changes to the Declaration of Helsinki. However, Dr Bankowski, the long-serving CIOMS Secretary General, refuses to provide any information about the proposed changes, the group authoring the new CIOMS guidelines, or the process governing the proceedings to change the guidelines, timelines or anything else related to this issue.

Considering the international importance of the CIOMS guidelines, this is nothing short of scandalous and wholly unacceptable. A new regime for the establishment of international research ethics guidelines is called for, that doesn't rely on anonymous, unaccountable organisations and experts that are chosen on the basis of unknown criteria.

A number of international clinical research efforts have disregarded the currently applicable international research ethics guidelines in vital respects. More than once, researchers have been caught red-handed and often red-faced by an alert international community of activists, concerned medical professionals and bioethicists. Unfortunately, the powerful US bioethics community's response has been to propose further dilutions of ethical standards in research instead of improving the standards of research clinical trials undertaken in developing countries. A US-based researcher, Henry Heimlich, injected live malaria parasites into HIV-infected people in the People's Republic of China after his research proposal was denied approval in the USA (4). This contravened CIOMS guidelines requiring that western researchers in developing countries provide clinical care meeting the standards of care in their home country.

In recent clinical trials (supported by a UN agency, UNAIDS), an antiretroviral agent already known in western countries to reduce HIV transmission from infected pregnant women to their foetuses was tested in developing countries — and compared to a placebo. To no one's surprise, the number of HIV-infected newborns was substantially lower in the group which received the active agent. The women in the placebo group were knowingly subjected to a lower standard of care (5). This violated the Declaration of Helsinki and the CIOMS guidelines requiring that research participants receive the best proven diagnostic and therapeutic services. Though scientists and UNAIDS argued that a placebo-controlled trial was needed to develop a cheaper drug regimen for people in developing countries, a placebo control was unnecessary for this purpose.

The CIOMS Guidelines require that the results of research undertaken in developing countries be made available (meaning affordable) to those communities in which the research took place. Justice-related considerations require that those who take on the burden of the research risks benefit from the results of their risk-taking. The trial is said to have demonstrated that a lower dosage of the drug in question worked to prevent HIV transmission from pregnant women to their foetuses. However, this knowledge has not translated into affordable access for millions of HIV-infected pregnant women in India, Southeast Asia, China, and Africa. The only winners were the pharmaceutical industry, for whom the trials were a world-wide marketing exercise, and individual researchers who managed to advance their careers by publishing the research results in academic journals.

There is ample evidence that informed consent is not taken seriously in many clinical trials western researchers undertake in developing countries. Medical journals regularly receive information from whistleblowers in the health-care profession about patients who were either not adequately informed, or who felt coerced into trials. (6)

Given that ethics in medicine is discussed more today than ever before, such reported failures to live up to basic

Udo Schuklenk, *PhD, Monash University, Centre for Human Bioethics, VIC 3168, Australia.*

ethics requirements should lead to improved standards in clinical research. On the contrary, as Peter Lurie, a medical researcher with the US voluntary organisation Public Citizen, points out, it is the same old story: "Write the rules, break the rules, get caught, change the rules." (7)

At the end of the 20th century, we are witnessing an unprecedented assault on research ethics standards. In April, the WMA's Council meeting in Santiago, Chile, discussed changes allowing researchers to operate on the basis of much lower research ethics standards in developing countries. The permissible use of placebo controls in clinical trials would be dramatically widened if the proposed changes came into effect. The WMA decided, however, that its national medical association members would be consulted after serious protests lodged by the British, Japanese and South African Medical Associations.

Most importantly, according to the proposed revisions of the Declaration of Helsinki and the CIOMS Guidelines, the standard of care to be provided by researchers to their subjects is determined by the standard of the community where the research takes place. In other words, western researchers testing a drug in a community too poor to provide its members basic medical care are under no ethical obligation to provide their subjects with even basic care.

The proposed changes also have implications for people living in western societies without universal health care. Participants in a clinical trial who can afford access to better (ie private) care will get better care than those who have to rely on basic (ie public) health care.

Delegates of national medical associations from developing countries do the ethical thing and reject the proposed changes during the next General Assembly of the WMA in October 1999. Readers of *Issues in medical ethics* who would like to receive further information, or who might contemplate supporting the efforts by Public Citizen to prevent the proposed watering down of the Declaration of Helsinki should contact the organisation's Dr Lurie at e-mail plurie@citizen.org. On a more general level, I would welcome proposals on how to make both the WMA and the CIOMS documents property of the international community of professionals and activists, rather than the property of democratically and professionally unaccountable organisations.

References :

1. Jonsen, AR, et al (eds): *Source book in bioethics*. 1998. Georgetown UP, Washington: 11-12.

2. Jonsen, AR et al. (eds): op.cit.: 13-15

3. Council of Medical Organisations of Medical Sciences: *International ethical guidelines for biomedical research involving human subjects*. CIOMS/WHO: Geneva, 1993.

4. Heimlich, HJ et al: Malaria therapy for HIV patients. *Mechanisms for ageing and development*. 1997. 93: 79-85.

5. Schüklenk, U: Unethical perinatal HIV transmission trials establish bad precedent. *Bioethics* 1998: 12: 312-319.

6. Karim, QA, Karim SSA et al. Informed consent for HIV testing in a South African Hospital: is it truly informed and truly voluntary? *American Journal of public health* 1998; 88: 637-640

7. Personal communication.