

## **Double Standards in Medical Research in Developing Countries**

By Ruth Macklin

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The field of biomedical law is a fascinating, but complex, area of law that continually faces new legal challenges, which in turn give rise to ethical controversies. Each new medical breakthrough requires extensive research to determine the safety and efficacy of a potential medical technology. Government groups, research and educational institutions, and pharmaceutical and biotechnology corporations fund and conduct most clinical trials. The diverging interests between those who want research to succeed for purely scientific and public health reasons versus those who seek to profit from successful trials present several ethical dilemmas. In her book, *Double Standards in Medical Research in Developing Countries*, Ruth Macklin tackles the exceedingly complex and irreconcilable debate over the need to balance advances in biomedical research with the obligations owed to research subjects and the greater populations in which research trials are conducted. Macklin's book is a survey of historical practices and controversies in the area of medical research and a provocative study of the current and future state of medical research in light of seemingly contrasting legal and ethical guidelines. Overall, this is a well-researched analysis of bioethics in international research, although many chapters are repetitive. The book ultimately disappoints the reader when, despite the author's expertise in the field, she fails to propose any practical solutions to current controversies.

Ruth Macklin is one of the founders of bioethics in the United States and a Professor of Bioethics at Albert Einstein College of Medicine. Prior to *Double Standards in Medical*

*Research in Developing Countries*, Macklin published *Against Relativism: Cultural Diversity and the Search for Ethical Universals in Medicine*, Oxford: Oxford University Press, 1999; *Enemies of Patients*, Oxford: Oxford University Press, 1993; and *Surrogates and Other Mothers: The Debates over Assisted Reproduction*, Temple University Press, 1994. In addition, Professor Macklin is the author of several articles published in professional and scholarly journals. Macklin's professional experience includes extensive international work as Vice President of Council for International Organizations of Medical Sciences, former president of the International Association of Bioethics, and Adviser to the World Health Organization. Additionally, President Clinton appointed Macklin to the Advisory Committee on Human Radiation Experiments and she has served on several committees for the National Institutes of Health.

*Double Standards in Medical Research in Developing Countries* begins by introducing the reader to the current controversies in international medical research, the inadequacy of international law in this area, and resulting ethical concerns. To effectuate advancements in medical technology, the medical and legal communities require that each experimental technology undergo rigorous screening and testing on animals and humans.<sup>1</sup> Clinical trials are conducted throughout the world for a variety of reasons, and this book highlights many of the motivations for conducting trials in developing countries where the laws are less stringent, if not altogether nonexistent.

International law governing medical research is sparse. Concepts such as “standard of care” and bioethics are culturally relative and thus vary widely among different regions of the

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<sup>1</sup> *Drug Approvals – From Invention to Market . . . A 12-Year Trip*, MEDICINET.COM, July 14, 1999 (outlining general clinical trials process and timeline), available at <http://www.medicinenet.com/script/main/art.asp?articlekey=9877>; See also Carol Rados, *Inside Clinical Trials: Testing Medical Products in People*, FDA CONSUMER MAG., (Sept. – Oct. 2003) available at [http://www.fda.gov/fdac/features/2003/503\\_trial.html](http://www.fda.gov/fdac/features/2003/503_trial.html).

world. Macklin very competently lays out the framework of the constant struggle within the international medical and legal communities to create universal research guidelines that protect the interests of developing countries. Much of this effort comes from groups within or associated with international organizations such as the World Trade Organization (WTO), the World Health Organization (WHO), and the United Nations, as well as many other international groups of less notoriety. By virtue of their influence and ability to effectuate sanctions, The WTO and WHO are perhaps in the best position to address the dichotomy between profit seeking motives and the pursuit of higher ethical standards. Competing interests and competing perspectives on ethical standards produce a stalemate and prevent resolution. Instead, much of the authority in this area is relegated to international bodies without any governing authority. These bodies publish advisory opinions, guidelines and “declarations” on a regular basis, however, despite their prestige and expertise, their end product is not binding upon researchers or private industry.<sup>2</sup>

Macklin addresses many ethical concerns throughout her book, most of which accompany one of two stages of research: during and after the trial. A recurring topic throughout *Double Standards in Medical Research in Developing Countries* is placebo-based clinical trials. In an effort to obtain the fastest and most useful results, researchers often conduct placebo-based trials whereby some research subjects receive the experimental new drug while others receive a placebo treatment, which in actuality is no treatment at all. By administering the new technology to some patients, and no treatment to others, the researchers are able to gauge the success, safety and efficacy of the technology quickly and accurately. The controversy arises when these placebo-based trials are conducted in developing countries when “best proven therapeutic

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<sup>2</sup> World Medical Association, *Declaration of Helsinki*, as amended by WMA 52<sup>nd</sup> General Assembly (Edinburgh 2000); Council for International Organization of Medical Sciences, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva 2002).

methods” are available elsewhere in the world. In effect, research subjects are permitted to continue to suffer, despite the availability of treatment, for the benefit of scientific research. In many cases, research under such conditions is not permissible in the United States or other developed countries. Researchers argue that placebo-based trials are necessary because the “best proven therapeutic treatment” will never be available to that population due to the cost of the technology, and conducting trials that may produce lower cost versions of a treatment justify this type of research. The second controversy relates to the post trial stage. In many cases, the research yields a beneficial treatment which is never made available to the research subjects who contribute to its success, nor to the greater population in the country where the research was conducted. Noticeably absent in international law are binding regulations on the testing of new medical technology and Macklin focuses much of the book on the standard of care owed to research subjects.

Macklin set out to address a very complex controversy with no clear cut or simple resolution. Her personal experience and knowledge, combined with her extensive research in the area of clinical trials, economics, law and ethics enables her to thoroughly present each side of the controversy. Macklin generally presents a well-balanced analysis of the issues before ultimately choosing a side with most of the issues she raises. Although there is no clear solution to the controversies discussed, the book raises the expectation that the author will present some coherent and practical proposal for how best to approach clinical trials in developing countries. On the contrary, the reader is left with the same ambiguity at the conclusion of the last chapter as after the first.

The underlying concern in the standard of care discussion is increasing access to medical treatment in the populations of developing countries. Ultimately, the best part of Macklin’s book

is the discussion of how governments have already made inroads towards providing cheaper drugs to populations who are most in need. In several cases, pharmaceutical companies have donated drugs to countries that are in dire straights. However, most healthcare personnel, government officials and economists agree that this only provides short term relief because eventually the donated supply will be depleted, leaving the population in substantially the same position as before. Another, more long-term, solution has been to establish differential pricing schemes where companies provide their products to developing countries at a fraction of the price the products are offered in developed countries. This too has its limitations, as even the reduced cost is often too burdensome for the populations of the developing countries. One of the most effective, yet highly controversial, schemes is compulsory licensing. Macklin's discussion of intellectual property rights in the international sphere was perhaps her best opportunity to present a practical solution to the issues raised in the book.

The struggle inherent in all of the international agencies' protocols is balancing the need to encourage and reward scientific research with the need to make medical technology available to developing countries. The WTO's Trade-Related Aspects of Intellectual Property Rights (TRIPS) requires all member countries to acknowledge patents held by pharmaceutical and biotechnology companies and requires member countries to pass laws that protect those patents.<sup>3</sup> At first glance, the WTO's stance on international patents appears to protect companies and to reward their innovative efforts at the expense of needy populations who cannot afford to pay premium prices for patented products.<sup>4</sup> However, the WTO's agreement contains an important

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<sup>3</sup> Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, LEGAL INSTRUMENTS – RESULTS OF THE URUGUAY ROUND vol. 31, 33 I.L.M 81 (1994). TRIPS provides for recognition of patent protection for 20 years, with some exceptions.

<sup>4</sup> Holly K. Towle & Shankar Narayan, *International Intellectual Property Licensing: Ten Points to Consider*, 806 PRACTICING L. INST. 1119, 1132 (2004). TRIPS provides for recognition of patent protection for 20 years, with some exceptions.

provision which permits countries to produce generic versions of patented drugs in the case of a “national emergency,” in which case the patent holder is paid a fair royalty for what essentially amounts to permissive infringement. While the term “national emergency” is ambiguous, this clearly opens the door to treat populations who are in dire need of crucial medical treatment.<sup>5</sup> This compulsory licensing scheme appears to be one of the best hopes for developing countries and it is a shame Macklin only briefly mentions its place in international research.

One of the main issues on which Macklin concentrates throughout her book is the ethical problem of conducting research in a developing country, using the local population as research subjects, and then failing to provide either the individual subjects or the larger population with post-trial treatment, particularly when the trials yield success. Pharmaceutical companies continually justify this reality by highlighting their inability to reconcile the cost of providing the drug with that population’s capacity to pay for it, even at a reduced cost. Private industry also argues that the developing countries lack the medical and healthcare infrastructure to safely and productively administer treatments. The compulsory licensing scheme, despite its adversarial nature to pharmaceutical companies, could help to rectify these problems. First, manufacturing of generic drugs can only be accomplished if some adequate manufacturing capability exists, and is only feasible if there exists a means to adequately distribute the products. Therefore, compulsory licensing only occurs in those countries where it is feasible and can serve as an impetus to enhance a country’s capacity to participate in compulsory licensing schemes.

Moreover, the pharmaceutical and biotechnology companies do not lose profits from a scheme

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<sup>5</sup> World Trade Organization, *Declaration on the TRIPS Agreement and Public Health*, Ministerial Conference, (Nov. 14, 2001). WTO officially took the position that a member country may waive the requirement that it respect a patent right in cases of extreme urgency or in cases of public non-commercial use. *See also* Holly K. Towle & Shankar Narayan, *International Intellectual Property Licensing: Ten Points to Consider*, 806 PRACTICING L. INST. 1119, 1132 (2004). The resulting compulsory license is non-exclusive, non-assignable, limited in time and scope, terminable under certain circumstances, and subject to adequate compensation to the patent holder.

that provides generic versions of their drugs to a market the companies never intend to target. Macklin briefly acknowledges the danger of parallel importation whereby the low cost generics could be exported to those markets served by the patented drug, which would slice into the companies' profits. Presumably, however, effective controls can be implemented that will obstruct such systematic distribution of drugs out of a country that truly needs them. While compulsory licensing may not resolve the extensive ethical concerns surrounding "double standards" in international research, it presents a potential practical solution that can go a long way toward evening the score between developed and developing countries by providing treatments to those most in need.

Macklin's book is thought provoking and has a tendency to nearly convince the reader that one viewpoint is obviously "correct," only to then present the opposing view in an equally compelling light. This effect is a testament to Macklin's ability to convey the difficulty in reconciling these controversies in international medical research. Unfortunately, despite her well-intentioned attempt to highlight the depth of ethical controversies, Macklin all but admits defeat for the effort to effectuate substantial change in the international research. Because both sides' interests are so adequately represented in international governing and advisory agencies, and there exists no discernable universal ethical standards, Macklin paints a bleak picture of any dramatic changes. In the absence of binding international law and regulations to address these larger ethical concerns, it seems only practical to utilize current laws in the most effective manner possible. Rather than be subjected to a defeat, the reader would be well served by a deeper analysis of the best current legal remedies and how they may be used as a stepping stone to achieve higher ethical standards in international medical research.