1-1-2008

Promoting Ethical Standards in Globalized Drug Trials through Market Exclusion

Fazal Khan
University of Georgia School of Law, fkhan@uga.edu

OP-ED

Promoting ethical standards in globalized drug trials through market exclusion

By Fazal Khan, Assistant Professor of Law, UGA

She was only ten years old and suffering from a serious infectious disease that was sweeping through West Africa, bacterial meningitis. But for this little girl and her family there was seemingly good news; there exists an effective treatment for bacterial meningitis, intravenous antibiotics. Further, once they arrived at the clinic in Kano, Nigeria, they saw Western doctors in white coats offering to provide medical treatment for free. And yet, three days later the girl died – not having received any proven antibiotic therapy, but only an experimental drug called Trovan.[1]

The family of the girl later claimed, along with many others, that instead of receiving proper medical care, they were unwitting participants in a multinational drug company's experimental trial that led to the death or serious impairment of numerous children.[2] But why would a drug company ever do something like this? Well, if data from the experiment helped the drug obtain market approval, and it became a market blockbuster, a company would have over a billion reasons.

The potential for tremendous financial reward generated by a newly approved drug provides a strong incentive for drug companies to move human subject testing to "developing countries," where minimal ethical guidelines and little transparency are the norm. The drug industry is acutely aware that there is minimal threat of costly civil and criminal legal sanctions for any of their ethical violations in impoverished countries. One study looking at drug trials in sub-Saharan Africa found that only 16 percent of these clinical drug trials met international ethical standards, despite 81 percent of them reporting oversight by an ethics review board. [3]

The globalization of clinical trials really became enabled after a 1980 Food and Drug Administration (FDA) ruling that allowed data from foreign trials to be used in new drug applications (NDA). Certain foreign studies used to support an NDA may opt to avoid direct FDA regulation, but must still satisfy FDA-imposed ethical standards – either the Declaration of Helsinki guidelines or regulations of the country where the research was conducted, "whichever represents the greater protection of the individual."[4]

Fazal Khan

The Declaration of Helsinki, an ethical code put out by the World Medical Association that governs research involving human subjects, has thus become the *de facto* international ethical standard. Therefore, in theory, under these FDA guidelines there should not be a "race to the bottom" problem, as an underdeveloped country's lax standards would automatically be upgraded to Declaration of Helsinki standards. And yet, we are still seeing consistent violations of ethical standards.

Globalization of the pharmaceutical industry and clinical drug testing is not necessarily a bad thing. Indeed, without this process, cures for seemingly intractable diseases like cancer or AIDS might not be possible in the near future. Further, many patients in the developing world might not have access to any medical attention at all, were it not for clinical drug testing. However, the real and potential benefits offered by globalization in the drug industry do not require us to silently accept violations of ethical standards or the absence of accountability and justice. As Nobel-laureate economist Amartya Sen has stated:

> Even though I'm pro-globalization, I have to say thank God for the anti-globalization movement. They're putting important issues on the agenda… My attitude to globalization is that one has to recognize first of all its inevitability, secondly its importance as an intellectual, social, political force, even as an economic force, but recognize that it can be very unjust and unfair and unequal, but these are matters under our control.[5]

In other words, even though the process may be inevitable, we are not powerless to control the actions of drug companies who conduct testing on human subjects in developing nations.

What can be done to address this problem? Multinational companies are notoriously difficult to regulate. By using multiple facilities around the globe, corporations can strategically evade state power and certain national regulatory schemes. From an international law perspective, the challenges are both "horizontal" and "vertical" in nature, and the legal responses can be "hard" or "soft."

For clinical drug trials, "horizontal" challenges constitute problems that arise between nations trying to regulate multinational drug companies that operate *across* international borders. "Vertical" challenges are problems with unethical trials that nations, more likely developing nations with limited resources, face *inside* their borders. "Hard-law" is represented by rule-based systems with binding authority on member states,

---

[1] Joe Stephens, *The Body Hunters: Exporting Human Experiments: Where Profits and Lives Hang in the Balance: Finding an Abundance of Subjects and Lack of Oversight Abroad, Big Drug Companies Test Offshore to Speed Products to Market,* WASH. POST., Dec. 17, 2000, at A1.

[2] *Abdullahi v. Pfizer,* 2002 U.S. Dist. LEXIS 17436.

[3] *See* David M. Kent et al., *Clinical Trials in Sub-Saharan Africa and Established Standards of Care: Systematic Review of HIV, Tubercolosis, and Malaria Trials,* 292 JAMA 237, 239 (2004).

[4] *See* 21 C.F.R. Sec. 312.120(5)(c)(1)(2005).

[5] Interview of Amartya Sen with David Barsamian accessed at http://www.indiatogether.org/interviews/sen.htm#part2.

> *"...The potential for tremendous financial reward generated by a newly approved drug provides a strong incentive for drug companies to move human subject testing to "developing countries," where minimal ethical guidelines and little transparency are the norm."*

such as the system in place under the World Trade Organization (WTO). "Soft-law" represents guidelines, practices, and policies generated by non-governmental organizations for voluntary self-regulation by industry or future adoption by states.

Addressing the ethical problems associated with globalized trials, some scholars have advocated a "hard, horizontal" approach, investing an international organization such as the World Health Organization (WHO) with binding authority to enforce ethical standards in clinical trials on a global basis. The problem with this approach is one of sovereignty and enforcement. Namely, how would an international organization enforce its decisions upon an unwilling sovereign nation?

Other commentators have argued for a "hard, vertical" approach with horizontal effects; that is, an expansive reading of the Alien Tort Statute (ATS) to allow U.S. courts to enforce foreign violations of ethical standards. However, after the U.S. Supreme Court's 2004 decision in *Sosa v. Alvarez-Machain*, it became more difficult for foreign plaintiffs to assert ATS claims. Indeed, the class of Nigerian plaintiffs who sued Pfizer in the U.S. over their Trovan drug trials (see *supra*) had their case dismissed for failure to state a cognizable ATS claim (the court indicated that their suit would be dismissed on *forum non conveniens* grounds as well). Thus, while the proposals discussed above advocate for more accountability and justice in globalized drug trials, it is unlikely that in practice they would offer more protection for vulnerable research populations.

A more feasible and effective strategy would be to use "horizontal, soft-law" measures such as increased monitoring and reporting on globalized drug trials that in turn could be used to enforce existing "hard-law" drug approval regulations vertically in lucrative markets such as the United States, Japan, and the European Union. The significance of these provisions is that drugs developed unethically could technically be excluded from the marketplace because of the impermissibility of the underlying clinical trials. Thus, if the fruits of unethical research were denied access to U.S., Japanese, or EU markets, it would have the same effect as a global prohibition, as no drug company would develop a drug in such a manner if they knew they would lose out on even one of these lucrative markets.

With the increasing accessibility of cheap internet communication, human research subjects and concerned citizens in developing nations can be empowered to effectuate much of the surveillance and monitoring activities of clinical drug trials. For instance, WHO could maintain a multi-lingual website for the reporting of alleged ethical violations. A credible report could then prompt WHO officials to obtain a sworn statement from the reporter, which would then trigger an investigation into the alleged ethical abuses. Verified reports of ethical abuses can then be taken into account by drug regulatory agencies when determining whether a drug should obtain market approval.

Rusk Center Staff

Newsletter design and illustrations:
mPrint Design Studio, mprintdesign.com

Edited by André B. Barbic