Bioethical Inquiry (2015) 12:101–106
DOI 10.1007/s11673-014-9596-2

ORIGINAL RESEARCH

Nonconsensual Clinical Trials: A Foreseeable Risk of Offshoring Under Global Corporatism

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Received: 1 December 2013 / Accepted: 17 November 2014 / Published online: 29 January 2015

Abstract This paper explores the connection of offshoring and outsourcing to nonconsensual global pharmaceutical trials in low-income countries. After discussing reasons why the topic of nonconsensual offshored clinical trials may be overlooked in bioethics literature, I suggest that when pharmaceutical corporations offshore clinical trials today, nonconsensual experiments are often foreseeable and not simply the result of aberrant ethical conduct by a few individuals. Offshoring of clinical trials is structured so that experiments can be presented as health care in a unique form of outsourcing from the host country to pharmaceutical corporations. Bioethicists' assessments of the risks and potential benefits of offshore corporate pharmaceutical trials should therefore systematically include not only the hoped for benefits and the risks of the experimental drug but also the risk that subjects will not have consented, as well as the broader international consequences of nonconsensual experimentation.

Keywords Consent · Pharmaceuticals · Clinical trials · Global health

Corporations, including multinational pharmaceutical corporations, increasingly dominate in partnerships with governments across the globe. This phenomenon, "global corporatism," requires a shift in the way bioethicists view global health issues, including pharmaceutical research. This paper explores how offshoring of experiments to low-income countries by pharmaceutical corporations and outsourcing of health care to pharmaceutical corporations by low-income host country government officials are connected to a lack of subjects' consent to participate in those experiments.[1] It then suggests that, under certain circumstances, a broader view be taken of the risks of experiments to include the foreseeable risk of nonconsensual experiments.

The significance of the risk of a lack of consent was recently evident when, in response to more than 200 different nonconsensual experiments, an Indian judge threatened in 2013 to stop all foreign clinical trials (experiments) in India because, he said, "[u]ncontrolled clinical trials are causing havoc to human life" (NDTV All India Agence France Press 2013, ¶3). The risk also has materialized recently in a Chinese firm's Artequick experiments in Comoros, in GlaxoSmithKline's (GSK) Varilix and Priorix tetra vaccines in Volgograd, Russia, and in its Synflorix vaccine experiments in Argentina and other Latin American countries. This risk has persisted long since bioethicists first became aware of consent problems in global pharmaceutical experiments and even after legal proceedings and worldwide media attention focused on Pfizer's notorious Nigerian Trovan experiments early in the 21st century.

After discussing reasons why nonconsensual offshored clinical trials may currently be overlooked in

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[1] Offshoring is the relocation of a business practice from one country to another; outsourcing is contracting work out to a third party.

contemporary bioethics literature, I suggest that when pharmaceutical corporations offshore clinical trials today, nonconsensual experiments are foreseeable and not simply the result of aberrant ethical conduct by a few individuals. Offshoring of clinical trials is structured so that experiments can be presented as health care, often by, or with the help of, government health officials in the low-income nations; this occurs through a unique form of outsourcing from host country officials to pharmaceutical corporations. Assessments of the risks and potential benefits of offshore corporate pharmaceutical trials should therefore systematically include not only the hoped for benefits and the risks of the experimental drug but also the risk that subjects will not have consented, as well as the broader international consequences of such nonconsensual experimentation. This kind of assessment requires a broader bioethical analysis than simply focusing on the risks and potential benefits of the experimental drug alone or on the potential economic or capacity-building benefits of such experiments.

Why the Foreseeable Risk of Offshored Nonconsensual Pharmaceutical Experiments May Be Overlooked

Nonconsensual pharmaceutical trials in low-income countries are not frequently addressed in current bioethics literature. They may currently be overlooked for several reasons. First, some bioethics scholarship on global human subjects research views consent as too "narrow" an issue to warrant continued attention. According to Ijsselmuiden and colleagues, "[o]ver the past 25 years, the ethics of international health research have shifted from addressing narrow issues such as … informed consent practices towards a greater emphasis on development and social justice" (Ijsselmuiden et al. 2010, 154). Similarly, Molyneux and colleagues write:

> Debates on the ethics of international health and health research have shifted over the last twenty five years away from a focus on the relevance and value of informed consent, towards considering broader challenges such as the potential for exploitation in international research, the need to make research responsive to local needs of host communities, and the implications of research for international relations and law (Molyneux et al. 2012, ¶1).

Such characterizations of consent as "narrow" are problematic because, ironically, they depend on overlooking some of what the scholars purport to be interested in when they justify shifting attention away from consent. Overlooked are the implications of nonconsensual research for international law (such as the United States Court of Appeals for the Second Circuit's recognition of nonconsensual human experimentation as a violation of customary international law under the Alien Tort Statute); the implications of nonconsensual research for international relations (such as legal action against the American corporation Pfizer by Nigerian authorities and against the British corporation GSK by Argentinian legal authorities); and the implications of evasion, through bribery, of consent requirements (punishable through the United States' *Foreign Corrupt Practices Act of 1977* and parallel European law). These international arenas are precisely the arenas used to justify a shift away from consideration of consent issues.

Second, nonconsensual trials may be underplayed if the absence of consent is conflated with less serious consent problems in international research. One problem with which the absence of consent might be conflated is consent that is not absent but less than fully informed. Another consent problem in international clinical trials with which a lack of consent may be conflated is the therapeutic misconception, which occurs when a subject to whom the experimental nature of an intervention has been disclosed nevertheless believes it is intended for her benefit. The absence of consent also may be conflated with manipulated consent, which occurs when the experimental nature of the intervention is disclosed to a patient, the patient is told that becoming a subject is the "price" she must pay in order to receive safe and effective medical treatment, and the patient then agrees to that condition. Each of these suboptimal types of consent is quite different from a complete lack of consent or consent based on deception. The latter occurred when the chief physician at a village health center in Grand Comore shouted through a megaphone during testing of Artequick by a Chinese corporation, "This drug is safe and effective. You are not being used a guinea pigs" (*The Economist* 2014, ¶16).

Third, some scholars may fail to distinguish among for-profit sponsors, contract research organizations, host country government officials, host country hospital officials, and host country health professionals, lumping them all together as researchers. This oversimplification masks the distinctive roles each plays, the incentives

under which each operates in the highly profitable global clinical trials business, and what is at stake for each should some individuals desire not to become subjects or have their family members become subjects. This view harkens back to a previous era in medical research when most trials were associated with academic medical centers and one could assume that research, not generation of profit, was the primary purpose of human experimentation. Dr. Chandra Gulhati, editor of the journal *Monthly Index of Medical Specialties*, emphasizes that incentives other than the desire to help generate knowledge can drive research: "Physicians are attracted by inducements of foreign travel, funds and fame. Of the four stakeholders—the sponsor or drug company, hospital, investigator and patient—three are on one side," says Gulhati. "They are only interested in getting the trial done" (Singh 2008, ¶4).

A Pattern in Offshored Nonconsensual Experiments When Drugs Are Unaffordable

What follows is a brief summary of three recently reported nonconsensual offshored clinical trials that fit a morally significant pattern. The experiment is offshored by a pharmaceutical corporation to a low-income country that has difficulty providing medicines to its population; in the host country, government and/or hospital officials and medical professionals are involved in negotiations with the pharmaceutical corporation and/or contract research organization; it is not those host country government and hospital officials but the poor and/or illiterate who are the experimental subjects; and these individuals and families expect to receive treatment but instead receive an experimental drug.

One example is GlaxoSmithKline's Synflorix vaccine trials in Argentina. This experiment took place in 2007–2008, using 13,000 Argentine infants, many allegedly without the consent of their parents. Babies were selected from poor families that sought medical treatment at public hospitals. A pediatrician reported the case to the Argentine Federation of Health Professionals and explained to the media how the selection process worked: "Once a picked patient arrives [he or she] would automatically disappear to be taken somewhere else in order to be treated by those doctors specially recruited by GSK" (Taján 2012, ¶10). Parents who objected were threatened. According to pediatrician Ana Marchese, "there already exist very good vaccines for the same disease, but we all know how laboratories work, they only care for their own business" (Taján 2012, ¶13). The president of the Argentine Federation of Health Professionals remarked, "These are people who depend entirely on the state apparatus and who are most often illiterate. They are vulnerable sections of society. They are unable to read any kind of consent form" (*The Telegraph* 2012, ¶6). An Argentinian judge fined British GSK as well as two of its contract physicians for, among other violations, falsifying parental authorizations. GSK appealed.

A second example occurred at the Bhopal Memorial Hospital and Research Center, which was set up on the directive of the Supreme Court of India with funds confiscated from Union Carbide to treat its victims following the Bhopal chemical disaster. Ramadhar Shrivastave, a 64-year-old survivor of the disaster was being treated at the hospital in 2007 for heart disease. He was given two bottles of unlabeled pills and was asked to sign a form that was written in English and which he did not understand. For about two years, the same physician phoned each month to remind him to get his pills. Each time, Mr. Shrivastave signed a form that contained the names and signatures of 10 to 15 other people who apparently also were subjects. He was never given any verbal or written details about the trial. After two years, the physician told him he did not need to come back. He learned from a local journalist in 2010 that he had participated in Astrazenica's Ticagrelor experiment. "I didn't even know what a clinical trial was until my son explained to me after all this came out," Mr. Shrivastave said.

> Of course I'm angry. I've been angry ever since I found out. But what can I do? We are poor people. If I had money I would have filed a case against them straight away, but we don't have money. If I'd known it was a drug trial I never would have agreed. How can I ever trust them again? These people should do trials on their own families, not poor people like me. God has saved me twice: first I survived the gas disaster and now this (Lakhani 2011, ¶37).

A third example occurred in the Kollam district Thiruvananthapuram government hospitals in India. A taxi driver tells of his parents, who were bussed to the hospital of the Kerala Institute of Medical Sciences

(KIMS). The parents were told that a physician would check for "sugar disease." They were then told that those who were found to have "sugar disease" would receive further treatment. The man's father was selected to receive an experimental drug instead of free treatment; the man's mother was not selected and received no medicine at all. The taxi driver believes that many groups were taken by bus for this kind of for medical experimentation (Indiavision 2012).

A Foreseeable Risk That the Experiment Will Be Nonconsensual

This pattern, involving offshoring to low-income host countries, agreements between pharmaceutical corporations and low-income country government hospital officials, experiments on the poor, and deception of experimental subjects, renders patients especially vulnerable to mistreatment, including, ultimately, nonconsensual pharmaceutical trials that are presented as health care. The repetition of the pattern also suggests that although nonconsensual experiments undoubtedly involve unethical conduct, such trials are not "flukes" or the result only of aberrant behavior by an occasional "bad apple"; they can be foreseen as a risk of this type of offshoring and outsourcing.

The offshoring of an experiment by a wealthy corporation to a low-income nation rather than to a wealthy or middle-income nation is a critical first step in the sequence of events creating the risk of a nonconsensual clinical trial. The pharmaceutical industry looks for sites where experiments can be done quickly, cheaply, and with minimal accountability for consent or other regulatory violations. Time and money are consumed by explaining to subjects, in their own language, that the intervention is an experiment—not safe and effective medical treatment—as well as by allowing for some potential subjects to receive the required information only to decline to enter the experiment. It is widely recognized that, in searching for offshore sites, pharmaceutical corporations look for lax regulatory environments, including lax consent enforcement, because this translates into opportunities for speedier enrollment of subjects than can be achieved in wealthier nations where potential subjects have better access not only to medicines but also to legal recourse should something go wrong. For years, legal scholars have decried the "enforcement vacuum" at every level of oversight for global clinical trials. Further deepening the legal void, in its 2013 *Kiobel v. Royal Dutch Petroleum Co*. decision, the U.S. Supreme Court limited the geographic reach of the only U.S. statute by which victims of nonconsensual clinical trials abroad had ever obtained compensation for their injuries, the Alien Tort Statute. The Supreme Court's decision ensured that pharmaceutical corporations (as well as other multinational corporations) would enjoy near legal immunity for acts abroad, making the global regulatory environment more hospitable to nonconsensual global experiments than it has been in more than a decade.

In the hosting low-income country, government and hospital officials and medical professionals bargain with pharmaceutical corporations and/or contract research organizations. There is little reason to think the outcome of negotiations between pharmaceutical corporations and host country negotiators would prioritize subject protections; too much else is at stake for the negotiators themselves. London and Zollman's (2010) auction metaphor captures the notion that, in these negotiations, low-income communities are competing with one another to gain access to the benefits of the clinical trials business. In choosing the site with the lowest cost–benefit ratio to the pharmaceutical corporation, there is a high likelihood of a race to the bottom in terms of not only benefits to the host community but also subject protections. London and Zollman concluded: "There is little reason to think the outcome would satisfy even minimal conditions of fairness" (London and Zollman 2010, 41). There is even less reason to think the outcome would prioritize subject protections. Under the competitive pressure of the negotiation process, host country negotiators who want to make their communities look attractive as venues for research may willingly cut subject protection corners in order to meet recruitment goals.

Bribery infects clinical trials and can erode subject protections at the negotiation phase. Idris Mohammed, head of the Nigerian Task Force to deal with the epidemic during which the well-publicized nonconsensual Trovan experiment took place in 1996, wrote:

> In the third world, authoritarian regimes and corrupt local government officials and health authorities are eager to be paid off by first-world organizations and to have good relations with them. They "encourage" entire villages or provinces to enroll in research programs while local doctors enrich themselves by providing human subjects (Mohammed 2007, 192).

The pharmaceutical industry, too, has a decades-long track record of international white-collar crime; the U.S. Department of Justice has warned that it is currently watching the industry for violations of the *Foreign Corrupt Practices Act*, presumably including bribery aimed at evading consent and ethics review requirements. One business commentator recently observed, however, that the industry "has a fraud habit that is just too profitable to kick" (Kelton 2013, ¶17). It is unlikely, therefore, that a requirement for subjects' consent would be allowed to stand in the way of a pharmaceutical corporation's race to be first to market.

Another part of the pattern is that it is poor and sometimes illiterate patients, not health officials or professionals, who arrive at the public clinic or hospital expecting to receive safe and effective treatment. Benatar and Fleischer's (2005) metaphor of "rental" is apt here. They write: "Clinical drug research is usually done on cohorts of public sector clinical and hospital patients who are essentially rented to the researcher" (Benatar and Fleischer 2005, 102).

Presenting experiments as if they were health care depends, finally, on a unique form of outsourcing. In the pharmaceutical industry, clinical trials are often outsourced from a pharmaceutical corporation to contract research organizations. In the kind of nonconsensual experiments of interest here, however, outsourcing is also done by host country health, hospital, and clinic officials and medical professionals. The task of obtaining and selecting medicines for the host community, made nearly impossible by the high cost of drugs, is contracted out to a third party, the pharmaceutical corporation or contract research organization.

What follows is deception, but it is not simply that; it is the materialization of a risk that is foreseeable under the conditions described here. At the clinical trials site, the effect of a global regime in which safe and effective drugs are already unaffordable (and will become increasingly so under the Trans Pacific Partnership's patent proposals) is to make "bait and switch" the path of least resistance. Poor patients are, of course, drawn to hospitals and clinics by the prospect of treatment, not by the prospect of becoming human subjects. But when drugs are financially out of reach, the tasks of obtaining and selecting drugs must be outsourced from host country officials and professionals to pharmaceutical corporations. A "switch" can be made to an experiment, if the experiment is presented to patients and families as health care. Recall how the selection process for the Synflorix vaccine experiment worked in Argentina: Babies who had been brought for safe and effective treatment would be picked for the study and disappear to be experimented upon by GSK's doctors. Similarly, the parents of the Indian taxi driver in the Kollam district boarded a bus expecting to receive treatment for "sugar disease"; but one received nothing and the other received an experimental drug.

If the risk that some experiments will be nonconsensual is foreseeable, how should bioethicists assess experiments in low-income countries? The breadth of social and international consequences considered should be no narrower than those that materialized from Pfizer's nonconsensual Nigerian Trovan experiment, about which the U.S. Second Circuit Court of Appeals wrote in one of the legal cases resulting from the experiment, *Abdullahi v. Pfizer*. The court identified far-reaching harms:

> [T]he Trovan trials in Kano apparently engendered such distrust in the local population that it was a factor contributing to an eleven month-long, local boycott of a polio vaccination campaign in 2004, which impeded international and national efforts to vaccinate the population against a polio outbreak with catastrophic results. According to the World Health Organization, polio originating in Nigeria triggered a major international outbreak of the disease between 2003 and 2006, causing it to spread across west, central, and the Horn of Africa and the Middle East, and to re-infect twenty previously polio-free countries (*Abdullahi v. Pfizer* 562 F.3d 163 [2009], at 187).

The risk assessment also should include dignitary harms to subjects used without their consent. The probability that any of these harms will materialize depends in part on the low-income country's legal and regulatory environments, its level of corruption, the economic incentives for local bureaucrats and health professionals, and the quality and enforceability of ethics committee review, if any. The probability of harm to subjects also depends on the track record of the particular pharmaceutical corporation in conducting nonconsensual experiments or, alternatively, in investing enough in consent to reasonably expect good practices.

Conclusion

Nonconsensual experimentation is a foreseeable risk of pharmaceutical corporations' practice of offshoring experiments in the manner described above. For such corporations, offshoring of clinical trials involves a search for speed, little accountability, and low prioritization of subject protections, and sometimes corruption. For host country health organizations and professionals, who have weak incentives to ensure consent and strong incentives to avoid it, presenting experiments as health care follows foreseeably from outsourcing to pharmaceutical corporations and contract research organizations the task of obtaining and selecting medicines.

Short of activism, bioethicists cannot change corporate globalization; it is largely beyond the reach of law and ethics. Nor can they change the practice of offshoring clinical trials. But bioethics scholars can assess human experiments in low-income countries realistically by treating nonconsensual experiments as a foreseeable risk of the offshoring system in a global regime where pharmaceutical corporations keep the cost of drugs high and their own accountability low. Rather than treating corporate offshore pharmaceutical trials as primarily benefits to be distributed, bioethicists should undertake a broad assessment of potential harms. Bioethicists should then incorporate those risks into their expectations of what offshore corporate pharmaceutical trials will bring to the world's poor.

References

Benatar, S.R., and T. Fleischer. 2005. Ethical and policy implications of clinical drug trials conducted in developing countries. *Harvard Health Policy Review* 6(1): 97–105.

Indiavision Online. 2012. Victims speak about medical experiments. August 17. Translated by S. Solomon. https://www.youtube.com/watch?v=agL6rB3yooI. Accessed December 1, 2014.

Ijsselmuiden, C.B., N.E. Kass, K.N. Sewankamdo, and J.V. Lavery. 2010. Evolving values in ethics and global health research. *Global Public Health* 5(2): 154–163.

Kelton, E. 2013. Is big pharma addicted to fraud? *Forbes*, July 29. www.forbes.com/sites/erikakelton/2013/07/29/is-big-pharma-addicted-to-fraud/. Accessed October 7, 2014.

Lakhani, N. 2011. From tragedy to travesty: Drugs tested on survivors of Bhopal. *The Independent*, November 15. www.independent.co.uk/news/world/asia/from-tragedy-to-travesty-drugs-tested-on-survivors-of-bhopal-6262412.html. Accessed October 7, 2014.

London, A.J., and K.J.S. Zollman. 2010. Research at the auction block: Problems for the fair benefits approach to international research. *The Hastings Center Report* 40(4): 34–45.

Mohammed, I. 2007. *Academics, epidemics and politics: An eventful career in public health*. Ibadan, Nigeria: Bookcraft.

Molyneux, S., S. Mulupi, L. Mbaabu, and V. Marsh. 2012. Benefits and payments for research participants: Experiences and views from a research centre on the Kenyan coast. *BMC Medical Ethics* 13: 13. doi:10.1186/1472-6939-13-13.

NDTV All India, Agence France Press. 2013. Drug trials in India "Causing havoc to human life": Supreme court. January 3. www.ndtv.com/article/india/drug-trials-in-india-causing-havoc-to-human-life-supreme-court-312763. Accessed 12, 01 2014.

Singh, M. 2008. Should clinical trials be outsourced? *Time*, August 7. http://content.time.com/time/health/article/0,8599,1830334,00.html. Accessed October 7, 2014.

Taján, J.C. 2012. GSK fined over vaccine trial; 14 babies reported dead. *Buenos Aires Herald*, January 3. www.buenosairesherald.com/article/88922/gsk-lab-fined-$1m-over-tests-that-killed-14–babies. Accessed December 1, 2014.

The Economist. 2014. Malaria eradication: Cure all? *The Economist*, January 25. www.economist.com/news/science-and-technology/21594956-novel-approach-using-drugs-instead-insecticides-may-make-it-easier. Accessed October 7, 2014.

The Telegraph. 2012. GlaxoSmithKline fined over trials on the babies of Argentinian poor. *The Telegraph*, January 11. www.telegraph.co.uk/science/science-news/9006614/GlaxoSmithKline-fined-over-trials-on-the-babies-of-Argentinian-poor.html. Accessed October 7, 2014.