

Health Rights Litigation Pushes for Accountability in Clinical Trials in India

CAROLIJN TERWINDT

Abstract

In 2009, around 24,000 girls in India were enrolled in a human papilloma virus (HPV) vaccination program that was later reviewed to investigate allegations of informed consent irregularities and inadequate monitoring. If the allegations are found to be correct, the clinical trial will have violated core human rights, including the right to health. Unfortunately, such irregularities are not unheard of in trials that are outsourced and off-shored. Those in charge of such clinical trials are, however, rarely held accountable before a court of law. As an example of health rights litigation, this article highlights proceedings before the Indian Supreme Court (“the Court”), which addresses the lack of protection of trial subjects. The Court already urged the Indian Government to advance the regulatory framework on clinical trials. However, full enforcement of relevant standards should not only address the role of state agencies, but also include private organizations conducting clinical trials and pharmaceutical companies that benefit from the results. An *amicus curiae* intervention in the ongoing Indian proceedings calls on the Supreme Court to clarify these standards and order European and American companies to comply.

CAROLIJN TERWINDT, MSc, LL.M, JSD, is a legal advisor at the European Center for Constitutional and Human Rights, Berlin, Germany.

Please address correspondence to Carolijn Terwindt. Email: terwindt@ecchr.eu.

Competing interests: None declared.

Copyright © 2014 Terwindt. This is an open access article distributed under the terms of Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

The problem: Lack of accountability in clinical trials

PHARMACEUTICAL COMPANIES DEVELOP medicines that may contribute to health and thus the companies can be “doing well while doing good.”¹ However, not everyone has equal access to the products of these companies because of the general inequality between and within countries. This unequal access to healthcare is not only problematic in and of itself; it also creates vulnerability in the process of enrollment in clinical trials.

Multiple international conventions guarantee people a right to enjoy the highest attainable standard of physical and mental health.² In keeping with these guarantees, clinical trials are well regulated. It is internationally recognized that one cannot carry out medical trials on people, subjecting them to a risk of personal injury, without first obtaining their informed consent.³ General Comment 14 to Article 12 of the International Covenant on Economic, Social, and Cultural Rights (ICESCR) states that the right to health “includes the right to control one’s health and body [...] and the right to be free from interference, such as the right to be free from torture, non-consensual medical treatment and experimentation.”⁴ Furthermore, the risks and benefits of clinical trials must be considered carefully before such trials are conducted, and the health of research subjects must be monitored carefully during and after trials.⁵ Monitoring clinical trials is essential to identify injuries and respond promptly.⁶

When clinical trials are not conducted in accordance with ethical standards, they infringe upon participants’ rights, including rights to informed consent and/or the right to health. There have been reports of these infringements from some clinical trials conducted outside the EU or the US.⁷ For example, in 1996, during a meningitis outbreak, the pharmaceutical company Pfizer tested a new drug, Trovan, on a group of young children in Nigeria. As is the case with many clinical trials, the children were divided into two groups, one receiving the drug Trovan and the other a moderate dose of

Ceftriaxone (a proven effective drug available at the same clinic). The negative side effects of Trovan were not detected by the staff at the clinic administering the drug. As a result, children whose health deteriorated or did not improve on Trovan were not switched to the alternative drug. The consequences were severe, and included long-term brain damage and six deaths.⁸

Despite media and NGO reports of irregularities in clinical trials in countries outside the EU or the US, few cases have come under judicial scrutiny.⁹ The Trovan case was an exception, and was taken to court in the US.¹⁰ After years of debate to determine the appropriate legal forum to hear the case, it was finally settled and the plaintiffs were awarded compensation. The settlement came, however, without admission of liability, and without creating binding jurisprudence regarding the relevant obligations of those conducting clinical trials.¹¹

A variety of private actors can be involved in the organization of a single clinical trial: pharmaceutical companies, academic institutions, contract research organizations (CROs), either commercial or non-profit, hospitals, and health professionals. Their legal obligations towards research subjects depend on their role, be it sponsor, investigator, or trial site owner/manager.¹² The sponsor is generally described, including in India, as the entity initiating, managing, and/or financing a clinical trial.¹³ The investigator is the person, with the necessary medical expertise, responsible at the trial site. The trial site is the facility at which a clinical trial is conducted.

Although the existing guidelines and legislation are detailed on the obligations of investigators, the obligations of trial sponsors are still developing.¹⁴ There is also remarkably little case law on the responsibilities of trial sponsors and what there is outlines the legal obligations of the investigators towards the trial participants and only in a few cases addresses the separate legal obligations of trial sponsors or the manufacturers of the tested drug or vaccine.¹⁵ In 2007, Mello and Joffe observed that

“courts have rarely considered the legal obligations that research sponsors owe to subjects.”¹⁶ Health rights litigation can and should continue to push towards clarifying and enforcing legal obligations.

This paper describes public interest litigation (PIL) petitions in India, which enable the Indian Supreme Court (the Court) to specify and enforce the legal obligations of parties responsible for and/or conducting clinical trials. It can also rule on the roles of foreign sponsors and manufacturers. The role of courts in home states has been examined as a forum for health rights litigation (based on the Trovan lawsuit), but this article describes a court case in India as an example of health rights litigation in host countries.¹⁷

The Court has been highly responsive to PIL petitions and has used its power to demand improvements in state regulation. It has not yet, though, taken any measures against private actors conducting clinical trials. Consequently, in one of these PIL proceedings, the European Center for Constitutional and Human Rights and the Essex Business and Human Rights Project submitted an *amicus curiae* brief, presenting an analysis of international guidelines, legislation, and jurisprudence, and outlining relevant legal obligations of trial sponsors and drug manufacturers.¹⁸

This paper presents an overview of key developments regarding clinical trials, describes the relevant PIL petitions before the Court, and discusses in detail a specific petition regarding the human papilloma virus (HPV) vaccination project, which was halted in 2010 after women’s rights activists drew attention to irregularities. It then identifies the obligations of clinical trial sponsors and develops a novel argument to impose a duty of care on the manufacturers of pharmaceutical products used in trials. It concludes that it is time that health rights litigation demands the enforcement of the obligations of foreign trial sponsors and manufacturers to protect research participants in countries outside the EU and the US.

Off-shoring and outsourcing of clinical trials

A clinical trial is a research study on human vol-

unteers to test the therapeutic effect of a new medication as well as identify side effects. Such trials are a necessary step to bringing drugs and vaccines into the market.¹⁹ Generally, there are four phases of clinical trials. Phase 1 concerns risk management and is done with healthy volunteers. Phase 2 aims to explore the therapeutic effect. Phase 3 aims to confirm the therapeutic effect, and Phase 4 is conducted after marketing approval and is intended to optimize usage of the drug and identify any less frequent or long-term side effects, or drug-drug interactions.²⁰

The growth of the pharmaceutical industry implies a need for increasing numbers of volunteers to take part in clinical trials. At the same time, caution in developed country populations makes it increasingly difficult to enroll people in trials.²¹ As a result, the globalization of clinical research during the past two decades has been documented, whereby multinational corporations from wealthier countries transfer stages of their research to less wealthy countries.²² This process is known as ‘off-shoring’; meaning pharmaceutical companies move their clinical trials outside their home country, most frequently to Brazil, China, India, or Eastern Europe. These countries can offer excellent medical centers at significantly lower cost than in the corporations’ home countries. The costs of clinical trials in some of the best local medical centers in India were one-tenth of what they would have cost in the US.²³ Frequently, pharmaceutical companies retain CROs to conduct the trial. During the past decade, this practice of ‘outsourcing’ has become more common and widespread.²⁴ It is estimated that about half the world’s clinical trials are now contracted out to more than 1,100 CROs.²⁵

Health activists have voiced concern about procedures used in these off-shored and outsourced trials.²⁶ The trials often occur in settings where health care is not easily accessible for all the population, which means that clinical trials can be viewed as a way to obtain health care that is otherwise unavailable or unaffordable. Furthermore, patients in these settings are less likely to question doctors’ suggestions or recommendations regarding participation in a trial. Lastly, conflicts of interest arise

easily when there is pressure to deliver results. For example, less care may be taken by those responsible for enrolling volunteers when their hospital budget is dependent upon the number of trial participants.

The practice of off-shoring and outsourcing clinical trials can make it difficult for trial participants to hold foreign trial sponsors or manufacturers to account if their rights are infringed. They face obstacles such as the lack of publicly available evidence, costs of litigation, and cultural and logistical issues.²⁷ As a result, cases are rarely heard in the home states of pharmaceutical companies. This paper, however, describes a unique collaborative effort in a case of health rights litigation involving foreign trial sponsors and manufacturers in the host state of India.

Health rights litigation arising from a vaccination project in India

In 2009, the states of Andhra Pradesh and Gujarat launched a vaccination project against HPV, some types of which can cause cervical cancer. The trial included girls aged 10-14 years who would receive the vaccination. The project had two components: a Phase 4 clinical trial of the HPV vaccination and observational research on the delivery of the vaccine. The project was designed and executed by PATH (Program for Appropriate Technology in Health), a US-based NGO, in collaboration with the Indian Council for Medical Research (ICMR) and the State Governments of Andhra Pradesh and Gujarat. Pharmaceutical company Merck developed and provided the vaccine Gardasil and GlaxoSmithKline developed and provided the vaccine Cervarix. The project was funded by the Bill and Melinda Gates Foundation. In April 2010, the Government of India suspended the program after women's groups, health activists, and some doctors questioned its rationale, ethics, and informed consent procedures, especially after the reports of deaths of some of the vaccinated girls.²⁸ At the time of the suspension, about 23,000 girls had already been vaccinated. The Indian Government set up an inquiry committee to look into the "alleged irregularities in the conduct of studies using HPV vaccine" by PATH in India.²⁹

The committee found that the process of informed consent was inadequate. It described the process whereby school principals signed consent forms on behalf of the children as "wrongful authorization." It also found that the monitoring system did not report all adverse events. The committee criticized the length of time for deaths to be made public, and that these were not investigated by an independent body even though it concluded the deaths were unrelated to the vaccine.³⁰ The committee found that the investigators "placed total reliance" on the routine program for the reporting and management of adverse events and that no independent mechanism was set up to verify the adequacy of the routine state program.³¹

Although the Indian Government set up the inquiry committee which found there were deficiencies in the planning and conduct of the study, this did not lead to any meaningful governmental action or sanction. As a result, the women's health activists who had brought the case to the attention of the Indian Parliament decided to take the case to court. Together with lawyers from the Human Rights Law Network (HRLN) in Delhi, they developed a petition.

In March 2010 and June 2011, women's groups and HRLN lawyers organized a fact-finding mission in the two regions where the HPV vaccination project was conducted. They visited schools where vaccinations were administered and conducted interviews with the wardens, teachers, students, and families. They investigated, for example, the informed consent process in an English secondary school run by the government, where approximately 300 girls were vaccinated. The fact-finders reported in the PIL petition:

The girls were not informed of the nature or purpose of the vaccine. The girls did not know where the cervix is located and this had not been explained to them. The girls believed the vaccination was being administered by the government. Many girls felt it was compulsory to be vaccinated. They were not informed of any possible side-effects of the vaccine.³²

On January 7, 2013, the Court admitted the petition for consideration. A second petition on the HPV vaccination project was filed by the Sama Resource Group for Women and Health, the Karnataka-based Drug Action Forum, and the Delhi Science Forum.³³

Public interest litigation on clinical trials before the Indian Supreme Court

The petitions in the HPV case were a timely follow-up to two other PIL petitions on clinical trials in India that had already enabled the Court to urge the Indian Government to improve protection of trial subjects.³⁴ In January 2013, the Court defined uncontrolled clinical trials of drugs on humans by multinational companies as “havoc” in the country, observing that the government had slipped into “deep slumber” in addressing this “menace.”³⁵ The Court criticized the negligence of the Ministry of Health and Family Welfare and the Central Drugs Standard Control Organization (CDSCO) for not addressing the issue, and asked for urgent action.³⁶ Complying with this order, on January 30, 2013, the government passed amendments to its regulation of clinical trials, providing, for example, easier access to compensation in case of injury or death by clarifying and broadening the category of trial-related injuries.³⁷

Further, on September 30, 2013, the Court suspended the approval procedure by the Drug Controller General of India concerning 162 new chemical entities, pending the introduction of efficient monitoring mechanisms.³⁸ On January 9, 2014, the CDSCO published a draft of new guidelines on audiovisual recording of the informed consent process in clinical trials.³⁹ Even though PIL has been criticized over the failure of legal decisions to be implemented, the Indian Government has so far answered the Court’s calls for improved regulation of clinical trials.⁴⁰

PIL petitions arise when the State has violated constitutional or statutory provisions.⁴¹ It is therefore not surprising that the Court primarily addressed the role of State organs as well as national legislation in the regulation of clinical trials. The PIL petitions on the HPV vaccination have, however,

also included the private actors PATH and (in one of the petitions) the two manufacturing companies as respondents. The Court accepted the petitions and immediately required a response from PATH. On August 12, 2014, the Court also issued notice to Merck and GlaxoSmithKline, thus also allowing the PIL proceedings to address the role of private actors in the protection of trial participants. Scholars have highlighted the complexity of the legal relationships among parties in clinical trials.⁴² Clearly, part of the responsibility lies with the individuals directly involved with the trial, such as the investigator. But what are the responsibilities of those initiating, funding, and managing clinical trials? And what are the responsibilities of the companies whose medicines are tested?

Because this case involved UK and US trial sponsors and manufacturing companies, the lawyers for the petitioners asked the European Center for Constitutional and Human Rights to submit an *amicus* brief to the Court outlining the legal framework on clinical trials in the respective home countries. The brief aimed to fill the gap created by the lack of judicial precedents. It provided an analysis of the relevant standard of care by reviewing a variety of sources: international treaties; international medical professional declarations; legislation and regulations from the EU, the UK, and the US; and jurisprudence on clinical trials, medical malpractice, and product liability. In addition, the analysis of standards drew upon the claims made by pharmaceutical companies in their codes of conduct and policy statements. Given the lack of case law in this area, the comparative analysis intended to assist the Court in determining relevant standard of care that can be expected from “reasonable corporations.”⁴³ The PIL proceeding may thus give the Indian Supreme Court the opportunity to address the obligations and liability of private actors in offshored and outsourced clinical trials.

The legal obligations of trial sponsors

As mentioned, it has become common for pharmaceutical companies to engage CROs to manage clinical trials involving the companies’ drugs and

vaccines.⁴⁴ While legislation does not always mention CROs explicitly, delegation of roles in the trials does not release the sponsor from its responsibilities, according to international medical declarations, the EU 2005 Good Clinical Practice Directive, and Indian Guidelines.⁴⁵

While some international medical guidelines elaborate on the obligations of investigators, they are generally vague on the obligations of trial sponsors.⁴⁶ This article focuses on two obligations which are particularly relevant to the HPV proceedings before the Supreme Court in India. Medical professional organizations, and legislation in both the US and the UK are in agreement that trial sponsors must verify that informed consent has been properly obtained, and must implement an adequate monitoring system. These obligations can be found in the Helsinki Declaration of the World Medical Association (Helsinki Declaration), Guidelines for Good Clinical Practice published by the International Conference of Harmonisation (ICH GCP Guidelines), and the International Ethical Guidelines for biomedical research involving human subjects of the Council for the International Organisation of Medical Sciences (CIOMS Guidelines). Even though these codes of conduct are not legally binding, they serve to “inform the court about what can be considered to be acceptable corporate behaviour.”⁴⁷ Moreover, these guidelines have informed the binding EU Directive on clinical trials from 2001, as well as domestic legislation in some countries, including the UK regulation on clinical trials and the Indian guidelines on good clinical practice. Finally, pharmaceutical companies, including Merck and GlaxoSmithKline, publicly claim to adhere to the Helsinki Declaration, CIOMS Guidelines, and the ICH GCP Guidelines.⁴⁸

The obligation on a sponsor to implement a monitoring system requires verification that the research protocol is followed, that adverse events are properly reviewed and reported, and that the trial complies with all regulations.⁴⁹ The obligation to monitor adverse events is central to clinical trials, not just to protect trial participants but also to determine if the medicine is safe for general

use. For this reason, monitoring is a component of international and Indian clinical trial standards and legislation.⁵⁰ For example, the US regulation on the Responsibilities of Sponsors and Investigators states that a “sponsor shall select a monitor qualified by training and experience to monitor the progress of the investigation” and “[t]he sponsor shall review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator.”⁵¹

Sponsors are also obligated to put measures in place so investigators take full and informed consent from research participants. Informed consent has to be obtained before any medical intervention (in general, not only clinical trials). It has been argued that the standard of care in clinical trials should be higher than in other medical interventions, especially if clinical trials are non-therapeutic.⁵² Sponsors have the responsibility to ensure informed consent is obtained properly, even though the process is executed by the onsite investigators.⁵³ This principle of informed consent derives from Article 1 of the Nuremberg Code, following the medical trial after the Second World War: “The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.”⁵⁴ Although these obligations are uncontroversial and are repeated in pharmaceutical company guidelines, there has been a lack of court cases addressing the liability of sponsors for failure of compliance.⁵⁵ Such cases could clarify what it means to implement a proper monitoring system, and what is necessary to verify that informed consent was given.

In a notable and exceptional precedent-setting judgment, a judge in Argentina addressed some of these questions in a case where he fined GlaxoSmithKline Argentina, S.A.⁵⁶ The company was the sponsor of a clinical trial in Argentina which tested the safety of the vaccine Synflorix against pneumococcal disease in children.⁵⁷ It was reported that in some instances, consent was given by parents who were minors themselves, or by grandparents who were not authorized to give consent for their grand-

children. One child was vaccinated even though the mother had expressly not given her consent, and there were instances where the signatures did not correspond to the individuals giving consent.⁵⁸ The Argentine Government drug authority fined the pharmaceutical company for failure to obtain appropriate informed consent.⁵⁹ GlaxoSmithKline appealed the fine, insisting it had complied with its duty of care to have a supervisory role over the principal investigators in the clinical trials.⁶⁰ The company used the defense that the alleged errors and poor documentation in the informed consent process could be regarded as a mere formality that did not pose any actual risk to the trial participants. The judge rejected the suggestion that “formal” mistakes and a lack of adequate documentation would not pose a risk to the health of research participants. He reasoned that even minor deficiencies in the procedure could become relevant later on, as certain health effects may only occur in the future.⁶¹ Therefore, the judge upheld the fine not only against the investigators but also against the trial sponsor. In upholding the fine against GlaxoSmithKline S.A., the Argentine judge confirmed and specified the supervisory duty of the trial sponsor regarding informed consent.

Health rights litigation, such as this case in Argentina, and the PIL petition in the HPV case in India, presents courts with the opportunity to provide a binding interpretation of the precise duties of sponsors to protect trial subjects.

Legal obligations of manufacturing companies

Whether or not pharmaceutical companies are sponsors in a clinical trial, they may have separate legal obligations as manufacturers (developers) and suppliers of the medicines under investigation in the trial. There is virtually no case law on this subject.⁶² However, the *amicus* brief offered to the Indian Supreme Court reasons that pharmaceutical companies have a duty of care towards trial participants according to the three-fold Caparo test of (1) foreseeability; (2) proximity; and (3) fairness. The Caparo test is recognized in common law as:

1. The harm must be a reasonably foreseeable result of the defendant’s conduct;
2. A relationship of proximity must exist between the defendant and the claimant;
3. It must be fair, just, and reasonable to impose liability.⁶³

Regarding foreseeability, the risk of injury can be distinguished from the risk of inadequate informed consent, and companies can foresee both. The nature of the clinical investigation of medicines carries risks for research subjects as adverse events may occur, and it is the purpose of clinical trials to identify these events. It is for this reason, too, that participants in clinical trials are insured, and that the EU Directive obligates companies to arrange for indemnification.⁶⁴ The risk of inadequate informed consent is also foreseeable, and pharmaceutical companies have publicly acknowledged this challenge. GlaxoSmithKline stated that in non-Western societies, “additional measures may often be needed to ensure the objectives of informed consent are met.”⁶⁵ Even in the absence of physical injury, a lack of informed consent is considered wrongful and injurious in itself. This was recognized, for example, in *Lugenbuhl v. Dowling* (a case involving medical treatment, not a clinical trial), where a lack of informed consent was proven, without physical damages or pecuniary loss. In that case, the Supreme Court of Louisiana in the US declared that “damages for deprivation of self determination, insult to personal integrity, invasion of privacy, anxiety, worry and mental distress are actual and compensatory.”⁶⁶

Regarding the second requirement of proximity, it can be seen as fulfilled because of the companies’ role developing and supplying the medicine for the clinical trial. The argument of proximity made in product liability cases is similar.⁶⁷ The Federal Court of Australia considered that “[b]y placing on the market a product to be consumed by end users, the manufacturer of a prescription medicine, no less than the manufacturer of any other product intended for human consumption, establishes the setting for the creation of the relationship of proximity from which the common law duty of care arises.”

Proximity is further established by the fact that the manufacturers (developers) of the medicine under investigation are the direct recipients of the scientific results obtained from the clinical trial, including the monitoring of adverse events. Moreover, courts have recognized that if there is risk of personal injury, the proximity-requirement may not be as strict as when the potential harm is economic loss only.⁶⁸ Thus, if a clinical trial leads to personal injury of a research participant, a duty of care can be imposed on a wider range of actors.

Finally, it can also be argued that the imposition of a duty of care is fair, just, and reasonable. It has been recognized that “the price of a bad outcome is exacted from the individual who suffers the untoward reaction, whereas the benefit of the breakthrough is available to society as a whole.”⁶⁹ Given that trial participants voluntarily participate in a risky process designed to improve and expand the medical repertoire within societies, it would only be fair, just, and reasonable to expect those whose product is tested in the clinical trials to bear a duty of care towards these subjects. This may be particularly so if the pharmaceutical company directly profits from the willingness of subjects to participate in clinical research.⁷⁰ Imposing such a duty can further be justified by reference to the information gap.⁷¹ Detailed knowledge of the risks and benefits of the medicine in the trial is only available to the manufacturers. Further, pharmaceutical companies have specific knowledge about clinical trials, the procedures of informed consent, and the possible risks involved, whereas trial subjects generally lack such knowledge.

The litigation in the HPV case enables the Indian Supreme Court to address the obligations that the manufacturing companies would have if such a duty of care were imposed. For example, what information did the companies provide regarding the vaccines, what risks did they know, which were disclosed, and did the companies verify that the trial participants were adequately provided with this information so that they could give their informed consent to participate in the trial?

Conclusion

The protection of participants in clinical trials requires regulation, including in trials that are outsourced and off-shored. For example, legislation could be used to ensure that only clinical trials that could benefit the local population will be approved. Legislation could also enshrine the right to post-trial access to treatment or to create an obligation to submit information to a clinical trial public registry. NGOs have drawn attention to the need for rules on placebo-controlled trials, and for trials to be limited to new classes of medicines rather than the ‘me-too drugs’ which do not provide clinical advantages over older drugs.⁷² Adequate compensation in the case of injuries or death is also necessary.

Informed consent and proper monitoring of adverse events are thus only two elements of a wider spectrum of needs and requirements that should be taken into account when assessing the protection of research participants everywhere in the world. Appropriate arrangements are even more challenging in countries without easy access to health care.

When ethical requirements for the protection of research participants are legally recognized, it becomes possible to demand their implementation through health rights litigation. The proceedings before the Indian Supreme Court on the HPV vaccination project is one example of health rights litigation that provides courts the opportunity to hold transnational companies accountable for not sufficiently protecting the rights of trial participants. This is exceptional, as there is very little case law on the obligations of trial sponsors and manufacturers. A judicial decision could strengthen the protection of trial participants by creating binding jurisprudence. It is, furthermore, one of the few cases that have been brought in a host country. Whereas the victims of the Trovan experiments took their case to court in the US to demand accountability of Pfizer and seek a settlement, the HPV proceedings seek to enforce standards and impose sanctions on the foreign trial sponsor and manufacturers directly in India. As India has shown a willingness to strengthen its regulations on clinical trials, such enforcement in the host country could set standards that would be exemplary for many other countries.

In August 2013, a parliamentary committee severely criticized PATH when it concluded that “its sole aim has been to promote the commercial interests of HPV vaccine manufacturers who would have reaped windfall profits had PATH been successful in getting the HPV vaccine included in the UIP [universal immunization program] of the Country.”⁷³ Given the wide disparities in access to health care in countries such as India, a lack of adherence to the relevant standards for the protection of clinical trial test subjects is deeply discriminatory. Without such compliance, pharmaceutical companies and CROs are far from ‘doing well while doing good.’ On the contrary, by not taking seriously their responsibility to secure the rights of test patients as outlined above, they may be guilty of violating human rights and exploiting the bodies of the poor and underprivileged for economic gain.

References

1. G. Heal, *When Principles Pay. Corporate Social Responsibility and the Bottom Line* (New York: Columbia University Press, 2008), chapter 5.
2. International Covenant on Economic, Social and Cultural Rights (ICESCR), G.A. Res. 2200A (XXI), Art.12. (1966). Available at <http://www2.ohchr.org/english/law/cescr.htm>; International Convention on the Elimination of All Forms of Discrimination against Women, G.A. Res. 34/180 (1979), Article 12(1). Available at <http://www2.ohchr.org/english/law/cedaw.htm>. International Convention on the Elimination of All Forms of Racial Discrimination, G.A. Res. 2106A (XX) (1965), Article 5e(iv). Available at <http://www2.ohchr.org/english/bodies/ratification/2.htm>. Convention on the Rights of the Child (CRC), G.A. Res. 44/25 (1989), Article 24(1). Available at <http://www2.ohchr.org/english/law/crc.htm>.
3. Article 1 of the Nuremberg Code, declared in: “Permissible Medical Experiments,” in *Trials of War Criminals before the Nuernberg Military Tribunals under Control Council Law No. 10: Nuremberg, October 1946–April 1949*. Washington: U.S. Government Printing Office (n.d.), vol. 2, pp. 181-182. Available at http://www.loc.gov/rr/frd/Military_Law/pdf/NT_war-criminals_Vol-II.pdf; International Covenant on Civil and Political Rights (ICCPR), G.A. Res. 2200A (XXI) (1966), Art. 7. Available at <http://www2.ohchr.org/english/law/ccpr.htm>.
4. Committee On Economic, Social And Cultural Rights, General Comment No. 14, 22nd session, UN Doc. E/C.12/2000/4(2000).
5. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice Guidelines (2005) [ICH GCP Guidelines] §5.1; European Parliament and European Council, Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the member states relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (2001) [EU Directive 2001], Article 3.2.a. Available at <http://www.eortc.be/services/doc/clinical-eu-directive-04-april-01.pdf>.
6. European Medicines Agency, *Better Vigilance for Public Health Protection. Overview of the New European Union Pharmacovigilance Legislation* (London: European Medicines Agency, 2013).
7. S. Lloyd-Roberts, “Have India’s poor become human guinea pigs?” *BBC News Magazine* (November 1, 2012). Available at <http://www.bbc.com/news/magazine-20136654>; Wemos Foundation, *The Clinical Trials Industry in South Africa: Ethics Rules and Realities* (Amsterdam: Wemos Foundation, July 2013). Available at http://www.wemos.nl/files/Documenten%20Informatief/Bestanden%20voor%20%27Medicijnen%27/Clinical_Trials_Industry_South_Africa_2013_v3.pdf; Wemos Foundation, *The Clinical Trial Industry in Kenya: Realities, Risks and Challenges*, (Amsterdam: Wemos Foundation, January 2014). Available at <http://www.wemos.nl/files/Documenten%20Informatief/Bestanden%20voor%20%27Medicijnen%27/Boekje%20Kenia%20%281%29.pdf>; Sama Resource Group for Women and Health, and Berne Declaration, *Exploratory Study on Clinical Trials Conducted by Swiss Pharmaceutical Companies in India: Issues, Concerns and Challenges*, (Lausanne/Zürich/New Delhi: Sama Resource Group, and Berne Declaration, September 2013).
8. S. Lee, “Informed consent: Enforcing pharmaceutical companies’ obligations abroad,” *Health & Human Rights: An International Journal* 12/1 (2010).
9. An exception has been the following case in the Netherlands: *Rechtbank Oost-Brabant*, January 16, 2013, case number 181812 / HA ZA 08-1953.
10. *Abdullahi v. Pfizer, Inc.*, 562 F.3d 163. (2d Cir. 2009).
11. B. Berkrot, “Pfizer settles remaining Nigeria, U.S. Trovan suits,” *Reuters*, February 23, 2011. Available at <http://www.reuters.com/article/2011/02/23/us-pfizer-idUSTRE71M18U20110223>.
12. J. Karlberg and M. Speers (eds), *Reviewing clinical trials: A guide for the ethics committee* (Hong Kong: Karlberg, March 2010), pp. 23-27. Available at http://www.pfizer.com/files/research/research_clinical_trials/ethics_committee_guide.pdf.
13. See, for example, EU Directive 2001 (see note 5), Article 2(e); The Medicines for Human Use (Clinical Trials) Regulations 2004, No. 1031 (United Kingdom) under (3); Good Clinical Practice Guidelines, Central Drugs Standard Control Organisation (CDSCO), Ministry of Health and

Family Welfare, Government of India. Available at <http://cdsco.nic.in/html/GCP1.html>.

14. Lee (see note 8).
15. See, for example, Hoge Raad der Nederlanden, Eerste Kamer, Nr. Co4/344HR, JMH/RM, 30 June 2006; *Daum v. Spine Care Medical Group Inc* (1997) 52 Cal.App.4th 1285 [61 Cal.Rptr.2d 260]; *Whitlock v. Duke University* 637 F. Supp. 1463 (M.D.N.C. 1986); *Haluska v. University of Saskatchewan* 53 DLR (2d) 436 (Sask CA 1965); Exceptionally, the obligations of a trial sponsor were subject of litigation in *Abney et al. v. Amgen, Inc.*; Cause No. 5:05-CV-254-JMH (E.D.Ky. filed June 21, 2005) and *Suthers et al. v. Amgen, Inc.*, Cause No. 05-CV-4158 (PKC) (S.D.N.Y. filed April 26, 2005). In these cases, the plaintiffs sued the trial sponsor in order to force it to continue providing them with the investigational drug. The Courts, however, reasoned that the informed consent form did not constitute a contract between trial subjects and the sponsor.
16. M. Mello and S. Joffe, "Industry sponsor obligations to their research subjects," *New England Journal of Medicine* 356/26 (2007), p. 2739.
17. Lee (see note 8).
18. *Amicus curiae* brief concerning non-state actor responsibility in clinical trials, November 22, 2013, submitted to the Supreme Court of India by the European Center for Constitutional and Human Rights and the Essex Business and Human Rights Project in Writ Petition (Civil) No. 558 of 2012, on file with ECCHR.
19. Karlberg and Speers (see note 12), p. 47.
20. *Ibid.*, pp.47-56.
21. J. Cekola, "Outsourcing drug investigations to India: A comment on US, Indian, and international regulation of clinical trials in cross-border pharmaceutical research," *Northwestern Journal of International Law and Business* 28, (2007-2008), p. 128.
22. S. Glickman et al., "Ethical and scientific implications of the globalization of clinical trials," *New England Journal of Medicine* 360/8 (2009), pp. 816-823; J. Rehnquist, *The globalization of clinical trials: a growing challenge in protecting human subjects*, Department of Health and Human Services, Office of Inspector General, OEI-01-00-00190 (2001). Available at <http://oig.hhs.gov/oei/reports/oei-01-00-00190.pdf>.
23. Glickman (see note 22).
24. *Ibid.*
25. Wemos 2013, (see note 7), p. 11.
26. For example, K.Seethi, "Clinical drug trials: Bioethics under siege," *Economic and Political Weekly* 36/34 (2001), pp. 3211-3213; J. Kahn, "India: A nation of guinea pigs," *WIRED Magazine* (March 2006). Available at <http://www.wired.com/wired/archive/14.03/indiadrug.html>; S. Nundy, M. Chir, and C. Gulhatti, "A new colonialism? Conducting clinical trials in India," *New England Journal of Medicine* 352/16 (2005), pp. 1633-1634; S. Srinivasan, *Ethical concerns in clinical trials in India: An investigation*, (Mumbai: Centre

for Studies in Ethics and Rights, February 2009). Available at http://www.fairdrugs.org/uploads/files/Ethical_concerns_in_clinical_trials_in_India_An_investigation.pdf; M. Huijstee and I. Schipper (eds), "Putting Contract Research Organizations on the Radar: An exploratory study on the outsourcing of clinical trials by pharmaceutical companies to contract research organizations in non-traditional trial settings," *SOMO, Salud y Farmacos, Centre for Studies in Ethics and Rights* (February 2011); I. Schipper, "Clinical trials in developing countries: How to protect people against unethical practices," (Directorate General For External Policies Policy Department, European Parliament, 2009), p.11. Available at http://www.europarl.europa.eu/RegData/etudes/etudes/join/2009/406974/EXPO-DEVE_ET%282009%29406974_EN.pdf.

27. *Ibid.*, pp. 38-45.
28. G. Mudur, "Human papillomavirus vaccine project stirs controversy in India," *BMJ* 340 (2010); G.Mudur, "Row erupts over study of HPV vaccine in 23,000 girls in India," *BMJ* 344 (2012).
29. Enquiry Committee, "Alleged irregularities in the conduct of studies using human papilloma virus (HPV) vaccine by PATH in India," Final Report of the Enquiry Committee appointed by the Govt. of India, Vide notification No.V.25011/160/2010-HR (February 15, 2011).
30. *Ibid.*, under 8.a.
31. *Ibid.*, under 6.1.10.
32. Public Interest Litigation Petition in the Supreme Court of India by Kalpana Mehta of Indore, Nalini Bhanot and V Rukmini Rao, filed on January 7, 2013, Para. 209.19.
33. "SC notice on vaccine trials," *The Telegraph* (November 12, 2013). Available at http://www.telegraphindia.com/1131112/jsp/nation/story_17557096.jsp#.UooBkifoCUK.
34. An earlier public interest litigation petition was filed by non-governmental organization Swasthya Adhikar Manch, Public Interest Litigation W.P.(C) No.33/2012 – Swasthya Adhikar Manch, *Indore v. Union of India*, filed on February 6, 2012. Another PIL petition on clinical trials was filed by Dr. Anand Rai, Times of India, "SC admits fresh PIL in clinical trial row," *Times of India*, Indore (March 20, 2012). Available at http://articles.timesofindia.indiatimes.com/2012-03-20/indore/31214534_1_drug-trials-pil-drug-controller-general.
35. "SC raps govt slumber on illegal clinical trials," *The New Indian Express* (January 4, 2013). Available at <http://newindianexpress.com/nation/article1406966.ece>; A. Buncombe, "A heaven for clinical trials, a hell for India: Court orders government to regulate drugs testing by international pharmaceutical companies," *The Independent* (September 30, 2013). Available at <http://www.independent.co.uk/news/world/asia/a-heaven-for-clinical-trials-a-hell-for-india-court-orders-government-to-regulate-drugs-testing-by-international-pharmaceutical-companies-8849461.html>.

36. V. Krishnan, "Ministry gets 2 months to define clinical trials regulatory regime," *Livemint* (January 22, 2013). Available at <http://www.livemint.com/Industry/JTitha6MKC-oQ1UdZToidFK/Ministry-gets-2-months-to-define-clinical-trials-regulatory.html>.
37. P. Chatterjee, "India tightens regulation of clinical trials to safeguard participants," *British Medical Journal* (2013), Vol. 346, f1275; S. Seethalakshmi, "Foreign companies stop clinical trials in India after government amends rules on compensation," *The Times of India*, Bangalore (August 1, 2013). Available at http://articles.timesofindia.indiatimes.com/2013-08-01/bangalore/40960487_1_clinical-trials-is-cr-suneela-thatte.
38. "Supreme Court stands firm on clinical trial ban," *The Health Site* (Editorial, October 22, 2013). Available at <http://health.india.com/news/supreme-court-stands-firm-on-clinical-trial-ban/>.
39. Central Drugs Standard Control Organization, Directorate General of Health Services Ministry of Health & Family Welfare, *Draft guidelines on Audio-visual recording of informed consent process in clinical trial*, January 9, 2014.
40. T. Khaitan, "From activist to alternative lawyering," National Law School of India University, Bangalore, paper on file with author.
41. Bakshi, *Public interest litigation* (Ashoka Law House: New Delhi, 2012), p.2.
42. Mello and Joffe (see note 17), p. 2739.
43. C. van Dam, "Tort law and human rights: Brothers in arms on the role of tort law in the area of business and human rights," *Journal of European Tort Law* 2/3 (2011), p. 244.
44. M. Shuchman, "Commercializing clinical trials—risks and benefits of the CRO boom," *New England Journal of Medicine* 357/24 (2007), p.1365; V. Roychowdhury, "CROs evolve to a new level," *Express Pharma* (April 2010). Available at <http://www.expresspharmaonline.com/20100415/market01.shtml>.
45. ICH GCP Guidelines (see note 5), section 5.2; Directive 2005/28/EC of 8 April 2005, article 7; Indian Guidelines for Good Clinical Practice, under 2.4.1.k (Principles of totality of responsibility). Available at: <http://cdsco.nic.in/html/GCP.html>; The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006, No. 1928 (United Kingdom), under (3)b. Only the US Code seems to imply that sponsors can transfer all obligations (United States Code of Federal Regulations, Title 21--Food and Drugs, Chapter I--Food and Drug Administration, Department Of Health And Human Services, Subchapter D--Drugs For Human Use, Part 312 Investigational New Drug Application, Subpart D--Responsibilities of Sponsors and Investigators, Sec. 312.52).
46. Lee (see note 8).
47. Van Dam (2011, see note 43), p. 237.
48. GlaxoSmithKline Government Affairs, Public Policy and Patient Advocacy, *Clinical Trials in the Developing World, Global Public Policy Issues, GlaxoSmithKline's Position* (2011). Available at <http://www.gsk.com/content/dam/gsk/globals/documents/pdf/GSK-on-clinical-trials-in-the-developing-world.pdf>; Merck, *Public Policy Statement: Clinical Trial Ethics* (March 2012), p.1. Available at http://www.merck.com/about/views-and-positions/clinical_trial_ethics_march2012.pdf.
49. Karlberg and Speers (see note 12), p. 24.
50. ICH GCP Guidelines (see note 5), §5.1; EU Directive 2001 (see note 5), Article 3.2.a; Indian Drugs and Cosmetics Rules 1945, Schedule Y, 2(2) i.
51. US Code Title 21, Chapter I, Subchapter D, Part 312, Subpart D (see note 48), Sec. 312.53; *Ibid.*, Sec. 312.56(c).
52. E. Haavi Morreim, "Medical research litigation and malpractice tort doctrines: Courts on a learning curve," *Houston Journal of Health Law and Policy* 4/1 (2003), p.41; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (United States Department of Health, Education and Welfare, 1978). Available at http://videocast.nih.gov/pdf/ohrp_belmont_report.pdf; *Whitlock v. Duke University*, 637 F. Supp. 1463 (M.D.N.C. 1986) pp. 1471-2.
53. *The Medicines for Human Use (Clinical Trials) Regulations 2004*, No. 1031 (United Kingdom), part 4, under 28(2); ICH GCP Guidelines (see note 5), §5.18.4 (e).
54. Nuremberg Code, declared in: "Permissible Medical Experiments," in *Trials of War Criminals before the Nuernberg Military Tribunals under Control Council Law No. 10: Nuremberg October 1946–April 1949*. Washington: U.S. Government Printing Office (n.d.), vol. 2, pp. 181-182. Available at http://www.loc.gov/rr/frd/Military_Law/pdf/NT_war-criminals_Vol-II.pdf;
55. GlaxoSmithKline Government Affairs, Public Policy and Patient Advocacy, "Clinical Trials in the Developing World, Global Public Policy Issues, GlaxoSmithKline's Position", 2011, available at: <http://www.gsk.com/content/dam/gsk/globals/documents/pdf/GSK-on-clinical-trials-in-the-developing-world.pdf>; GlaxoSmithKline, "One company, one approach," *Code of Conduct*. Available at <http://www.gsk.com/content/dam/gsk/globals/documents/pdf/Policy-Code-Conduct.pdf>; Merck, "Public Policy Statement: Clinical Trial Ethics," March 2012. Available at http://www.merck.com/about/views-and-positions/clinical_trial_ethics_march2012.pdf.
56. A. Gerlin, "Glaxo to Appeal Fines in Argentina Case Over Synflorix Trial," *Bloomberg Businessweek*, January 3, 2012, available at <http://www.businessweek.com/news/2012-01-03/glaxo-to-appeal-fines-in-argentina-case-over-synflorix-trial.html>. Causa No 925/2011, GlaxoSmithKline Argentina S.A. – Abate Héctor – Tregnaghi Miguel S/Infracción Ley 16.463 del Registro de la Secretaría No 4 del Juzgado Nacional en lo Penal Económico No 2, Buenos Aires (December 28, 2011), part II. Available at <http://www>.

mdzol.com/files/content/353/353381/Fallo_Aguinsky.pdf.

57. Gerlin, “Glaxo to Appeal Fines in Argentina Case Over Synflorix Trial,” *Bloomberg Businessweek* (January 3, 2012). Available at <http://www.businessweek.com/news/2012-01-03/glaxo-to-appeal-fines-in-argentina-case-over-synflorix-trial.html>.

58. Causa No 925/2011 (see note 61), under II.

59. *Ibid.*

60. Causa No 925/2011 (see note 61), part II; *La Gaceta*, “La polémica vacuna ya estaba en el mercado,” *La Gaceta* (4 January 2012). Available at <http://www.lagaceta.com.ar/nota/472066/sociedad/polemica-vacuna-ya-estaba-mercado.html>.

61. Causa No 925/2011 (see note 60), under V.

62. In one case, the plaintiffs did allege that manufacturer AstraZeneca was responsible for the harm resulting from a clinical trial. The judge dismissed the claim due to a lack of causation. This might imply that the judge did accept the imposition of a duty of care, but this was not made explicit (*Mary Weis v. Board of Regents for the University of Minnesota*; Dr. Stephen C. Olson; Dr. Charles Schulz; Institutional Review Board for the University of Minnesota; AstraZeneca Pharmaceuticals LP; AstraZeneca LP; and Zeneca Inc., Court File No.27-CV-07-1679, District Court, State of Minnesota, Order and Memorandum Granting Partial Summary Judgment, 11 February 2008, p.13. Available at http://www.circare.org/dw/27cvo71679_order_20080211.pdf.

63. *Caparo Industries PLC v. Dickman & Ors* [1990] UKHL 2 (February 8, 1990).

64. EU Directive 2001 (see note 5), article 3.2.f.

65. GlaxoSmithKline, 2011 (see note 51).

66. *Lugenbuhl v. Dowling*, 701 So 2d 447, 455-56 (La. 1997). Available at http://www.leagle.com/decision/19971148701So2d447_1880; See also *Haluska v. University of Saskatchewan* 53 DLR (2d) 436 (Sask CA 1965).

67. *Peterson v. Merck, Sharpe & Dohme (Aust) Pty Ltd* ([2010] FCA 180), Part VII, No 793-794.

68. *Grimes v. Kennedy Krieger Institute, Inc.*, 366 Md. 29, 782 A.2d 807 (Md.2001), p. 842.

69. An unknown author is cited here by K. Morin, “The Standard of Disclosure in Human Subject Experimentation,” *The Journal of Legal Medicine* 19/2 (1998), p. 157, quoted in *Grimes v. Kennedy Krieger Institute, Inc.*, 366 Md. 29, 782 A.2d 807 (Md.2001), p. 838.

70. *Grimes v. Kennedy Krieger Institute, Inc.*, 366 Md. 29, 782 A.2d 807 (Md.2001), p. 846, footnote 36.

71. C. van Dam, *European tort law, second edition* (Oxford University Press, 2013), p.245.

72. Wemos 2013 and Wemos 2014, (see note 7); “Light and Lexchin, Pharmaceutical research and development: What do we get for all that money?” *British Medical Journal* 2012; 345:e4348.

73. Parliamentary Standing Committee, *72nd Report on alleged irregularities in the conduct of studies using Human*

Papilloma Virus (HPV) vaccine by PATH in India, Department of Health Research, Ministry of Health and Family Welfare (August 2013), para. 7.13.