

### **Human rights violations in clinical trials in India, the case of the HPV vaccination project**

In 2009, the States of Andhra Pradesh and Gujarat launched a research project for the vaccination against the human papilloma virus (HPV) which can cause cervical cancer. Adolescent girls between the ages of 10 – 14 in the States of Andhra Pradesh and Gujarat were to be vaccinated. The vaccines were provided by GlaxoSmithKline and Merck. The project was designed and executed by PATH (Program for Appropriate Technology in Health) and funding was received from the Bill & Melinda Gates Foundation. In April 2010, however, the Government of India suspended the program as several violations of ethical standards by PATH were widely reported by human rights organizations. However, by that time, 24,000 girls were already vaccinated.

In 2011, a parliamentary enquiry committee found that the process of informed consent was inadequate (especially questioning the fact that school head masters signed consent forms on behalf of the children, calling it “wrongful authorization”). Informed consent is the process in which trial volunteers are informed about the nature, significance, implications and risks of the trial. Informed consent is crucial to protect people against unwanted experimentation. Also, in the absence of personal physical injury, Article 7 of the International Covenant on Civil and Political Rights (ICCPR) recognizes that a lack of informed consent constitutes a human rights violation: “*No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation.*” The parliamentary committee further criticized that the monitoring system did not report all adverse events. Monitoring of clinical trials is, however, essential to identify injuries and respond promptly and adequately.

While the project was ostensibly intended to benefit the Indian population, in August 2013, a second parliamentary committee severely condemned PATH as 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*” (72<sup>nd</sup> Report, Department of Health Research, Ministry of Health and Family Welfare, Para. 7.13).

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### **Outsourcing and off-shoring of clinical trials**

A clinical trial is a research study on human volunteers to test the therapeutic effect of new medication, as well as the possible negative side effects. Such trials

are a necessary step in order to bring drugs and vaccines on the market. The growth of the pharmaceutical industry implies a need for an increasingly large number of volunteers. At the same time, the caution of the western population makes it more difficult to enroll people. European and North-American pharmaceutical companies have begun to shift a substantial part of their clinical trials to countries like Brazil and India. These countries can offer excellent medical centers, while at the same time the costs are less than in the home countries. Frequently, companies retain contract research organizations to conduct the trial on the ground.

Health activists have voiced concern about the procedures in these ‘off-shored and outsourced’ trials. They often occur in settings where healthcare is not easily accessible for the ordinary population, which means that clinical trials can be viewed as a way to obtain healthcare which is otherwise unavailable or not affordable. Furthermore, doctors tend to be held in high regard, which means that patients are not likely to question the suggestions made by medical professionals. Lastly, conflicts of interests easily arise under the pressure to deliver results. Less care may be taken by those responsible for enrolling volunteers, for example, when their hospital budget is dependent on the number of trial participants. In particular, irregularities in obtaining informed consent of vulnerable populations have been criticized.

If clinical trials are not conducted according to the highest ethical standards, they may infringe upon the right to informed consent and the right to health. ECCHR believes that the role of transnational enterprises in causing or contributing to human rights violations should be investigated. However, despite frequent reports of irregularities in clinical trials in newspapers and NGO publications, few cases have come under judicial scrutiny. It has been recognized that the practice of off-shoring and outsourcing clinical trials can make it difficult for trial subjects to hold foreign trial sponsors or manufacturers accountable if their rights are infringed. This is due to obstacles such as the lack of publicly available evidence, financial costs of litigation and cultural and logistical issues.

Therefore, ECCHR welcomes the ongoing proceedings which enable the Supreme Court in India to confirm and enforce the obligations of those undertaking clinical trials, especially also taking into account the roles of foreign sponsors and manufacturers.

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## **Seeking a judicial decision on the liability of the trial sponsors and manufacturers of the vaccines**

Women’s health activists decided to take the case to court and in January 2013 they filed a public interest petition (PIL) at the Indian Supreme Court. Since then, the Court has urged the Indian government to advance the regulatory framework on clinical trials and improve its system of approval of licenses. Not yet fully addressed, however, is the role of the non-state actors in the protection

of trial participants. What are the responsibilities of those initiating, financing and conducting clinical trials? What are the responsibilities of the manufacturers whose drug or vaccine is tested? Scholars have highlighted the complexity of the legal relationships among parties in clinical trials. This petition on the HPV vaccination project gives the Indian Supreme Court the opportunity to address the obligations and liability of these non-state actors.

Given the lack of judicial precedent, ECCHR decided to submit an Affidavit to the Indian Supreme Court. ECCHR's report outlines the obligations of trial sponsors and manufacturers based on a review of relevant standards that are developed in international treaties and declarations; as well as relevant legislation and jurisprudence, mainly from Europe (in particular the UK) and the United States, where the non-state respondents have their headquarters. This comparative analysis can inform the standard of care that can be expected from "reasonable corporations."

The lack of informed consent and the lack of monitoring constitute violations of the right to be free from cruel, inhuman or degrading treatment and the right to health. It has been recognized that states may breach their international human rights law obligations where such abuse can be attributed to them, or where they fail to take appropriate steps to prevent, investigate, punish and redress private actors' abuse. The Indian Supreme Court's ruling in the HPV case could order such investigation, provide access to an effective remedy, and thus increase the protection of trial subjects.

There is remarkably little case law on the responsibilities of those undertaking clinical trials. The Court's ruling regarding the HPV vaccination project can thus serve to develop the jurisprudence in this regard to clarify and enforce the different obligations of sponsors, manufacturers, and clinical research organizations in clinical trials. As there is even less case law on the responsibilities in trials conducted in third countries, the Court's ruling can additionally serve to clarify and enforce transnational obligations.

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## **Legal obligations of sponsors and manufacturers**

A trial sponsor is generally described as the entity initiating, managing and/or financing a clinical trial. According to international medical guidelines and legislation from the EU, UK, and US, sponsors have the obligation to implement a proper monitoring system to verify that the research protocol is followed, that adverse events are properly reviewed and reported, and that all regulations are complied with. ECCHR further concludes that sponsors have the obligation to put and keep in place arrangements for the purpose of ensuring or verifying that informed consent was taken properly.

Regarding the obligations of drug manufacturers, based on an analysis of general tort principles, ECCHR reasons that they owe a duty to take reasonable measures

to ensure that the trial subjects have access to correct and sufficient information regarding the expected benefits and possible risks posed by the relevant drugs or vaccines. A duty of care can be imposed as the companies can foresee the risk of injury as well as the risk of inadequate informed consent. There is sufficient proximity between the companies and the trial subjects, because the companies develop and supply the investigational medicinal product. Lastly, given that trial subjects voluntarily participate in a risky process designed to improve the medical repertoire of 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. Furthermore, if the Court finds that the parent companies knew its products would be used in the trial and indeed even ‘partnered’ in the vaccination project, there could be grounds to hold them liable in addition to their Indian subsidiaries.

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## Special care for vulnerable trial subjects

In the HPV case, special care in guaranteeing the right to health and the right to informed consent was required by three separate human rights conventions. The trial subjects were young girls between 10-14 years old, and several of them were from tribal backgrounds. They were therefore entitled to special care under the Convention on the Rights of the Child, the Convention on the Elimination of All Forms of Racial Discrimination and the Convention to Eliminate All Forms of Discrimination Against Women (CEDAW). Legal commentators have emphasized the intersectional discrimination frequently experienced by young girls or rural women.

Article 12(1) CEDAW protects the right to non-discriminatory access to health services. Adequate access to health services includes the availability of information about the services, such as the risks and benefits of possible options, which is central to informed decision-making. CEDAW commentators emphasize that informed consent is essential to protect the human dignity of women. It should thus be verified, if the girls, their parents, and legal representatives were provided with sufficient information regarding cervical cancer, the risks and benefits of the HPV vaccine, and the alternative possibilities to screen for cervical cancer. If such information was not properly provided, this would constitute discrimination against women under Article 12 of CEDAW. According to CEDAW’s General Recommendation, the State’s obligation to protect rights relating to women’s health “*requires States parties, their agents and officials to take action to prevent and impose sanctions for violations of rights by private persons and organizations*” (No 24, Para.15).

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