

# Features

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## Transnational pharmaceutical companies' clinical drug trials in Egypt: ethical questions in a challenging context

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*“A company’s clinical trials should observe the highest ethical and human rights standards, including non-discrimination, equality and the requirements of informed consent. This is especially vital in those States with weak regulatory frameworks.”*

UN Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines<sup>1</sup>

Over the past two decades, the location of clinical drug trials sponsored by transnational pharmaceutical companies has shifted from affluent Western countries to low- and middle-income countries. Among the top emerging pharmaceutical markets – so-called ‘pharmerging countries’<sup>2</sup> – Egypt has become a popular destination for clinical trials, with the number of clinical drug trials in Egypt nearly tripling between 2008 and 2011.<sup>3</sup> The Arab spring events of early 2011 and the subsequent political unrest had no chilling effect on the number of active international drug trials – on the contrary. A major concern is that due to the absence of a robust legislative framework for clinical trials and the subsequent absence of sufficient independent oversight and monitoring by the Egyptian authorities, there is an increased risk of vulnerable patients not being adequately protected and being exploited as trial participants.<sup>4</sup> Note that all research information has been extracted from the report compiled and published by SOMO, Wemos, Public Eye in June 2016.

### The attractiveness of Egypt for drug trials

Egypt, as a clinical trial location, provides distinct ‘advantages’ to pharmaceutical firms, similar to those in better-known offshoring destinations, such as India or China. First, patient recruitment is relatively easy and cheap. Egypt’s population is growing fast and has a large pool of patients with a wide range of diseases that are attractive for drug testing: there is a high prevalence of cancer, and the prevalence of hepatitis C in Egypt is the highest in the world. Second, a large portion of the population can be described as ‘treatment-naïve’, i.e. individuals who have not received earlier treatment for a given illness. Finally, recruitment of trial patients is easier due to the lack of affordable treatments. Egypt also has an attractive infrastructure (e.g. hospitals and staff) required for conducting trials, and price levels for trials are far lower than in Western countries.

In February 2016 57 active drug trials were registered in Egypt, compared to 200 in South Africa (one of the most popular clinical trial locations in Africa).<sup>5</sup> Twenty-one international pharmaceutical companies were running trials, however just two Swiss companies – Novartis and Roche – sponsored almost half of all trials. Trials were predominantly focused on cancer, with over half of all international active drug studies being cancer trials, followed far behind by infectious diseases (10%, mainly hepatitis C trials) and metabolic disorders (10%, mainly diabetes).

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1 Published in the report to the General Assembly of the UN Special Rapporteur on the right to the highest attainable standard of health (UN document: A/63/263, dated 11 August 2008). [www.who.int](http://www.who.int) (Accessed 11.12.2016)

2 IMS Institute for Healthcare Informatics (2015): Global Medicines Use in 2020: Outlook and Implications. [www.imshealth.com](http://www.imshealth.com) (Accessed 1.3.2016)

3 Matar A, Silverman H. (nd): Perspectives of Egyptian Research Ethics Committees Regarding Their Effective Functioning. *Journal of empirical research on human research ethics: JERHRE*. 2013;8(1):32-44. doi:10.1525/je.2013.8.1.32. [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov) (Accessed 28.2.2016)

4 All research information has been extracted from the report compiled and published by SOMO, WEMOS, Public Eye (2016): Industry Sponsored Clinical Drug trials in Egypt. June. [www.somo.nl](http://www.somo.nl)

5 US National Institute of Health (nd): Clinical Trials registry. [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (Accessed 11.12.2016)

Clinical trial participant  
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### Ethical guidelines and regulations

Clinical trial participants provide a great service, putting themselves at risk to establish whether a treatment is safe and effective for others. Ethical guidelines exist to protect these people.<sup>6</sup> The leading international ethical standards applicable to how pharma companies should conduct of clinical trials in low- and middle-income countries are the Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS) Guidelines. These guidelines stipulate that every clinical trial participant is entitled to the highest possible standard of care, where this is not possible it is considered unethical and exploitative to run tests in that country.<sup>7</sup> The guidelines refer specifically to vulnerable groups – including that specific safeguards should be in place to protect the rights and welfare of vulnerable persons; the research should be justified as responsive to the needs of this group and unable to be carried out in a non-vulnerable group, additionally this group should stand to benefit.<sup>8</sup>

Although Egypt lacks a robust legislative framework for clinical trials, there are some regulations that address experimenting on humans. The most relevant to mention here is the regulation that prohibits the use of foreign pharmaceutical products in clinical trials that are not approved in their country of origin (law 127/1955 of practicing pharmacy, article 59).

### Unethical practices

One of the pillars of ethical clinical trials is ‘informed consent’. In Egypt, the lack of access to standard treatment – due to the high proportion of people living in poverty and a public health insurance system that covers only half of the population – means that people who are seriously ill have little choice but to participate in risky clinical trials in order to access free (but experimental) treatment. To receive treatment, participants will sign up despite the risks, making their consent neither voluntary nor informed. The Coordinator of the Commission for Defending the Right to Health goes as far as to say, that the informed consent of a volunteer is meaningless in Egypt, given the high rates of poverty. For example, one of the cancer patients in the study noted, “I was so happy to have an opportunity for treatment after having lost hope. I signed the informed consent form immediately and did not care to read it in detail.” The side effects and risks of clinical trials can also be unclear to these patients and treatment for the side effects can be costly and the pain unbearable. According to the Declaration of Helsinki, this constitutes an ethical violation. In fact, the lack of access to treatment and economic vulnerability defines these patients as vulnerable and therefore unfit for a standard informed consent process.

The cancer trials in particular (constituting the majority of the trials in Egypt), show the vulnerability of Egyptian trial participants and the dichotomy of treatment received in contrast to cancer patients in high-income countries. In affluent countries, cancer patients receive a proven standard treatment first. Experimental treatments are regarded as the last option. For some Egyptian cancer patients, the experimental treatment is their only option, which means that the best-proven treatment is denied to them. This is unethical and exploitative according to leading ethical guidelines.

6 Department of Health and Human Services (nd): Patient recruitment: Ethics in clinical research. <https://clinicalcenter.nih.gov> (Accessed 11.12.2016)

7 Ravinetto, R et al (2014): Globalisation of clinical trials and ethics of benefit sharing. *The Lancet Haematology*, Volume 1, Issue 2, e54–e56. [www.thelancet.com](http://www.thelancet.com) (Accessed 31.5.2016)

8 World Medical Association (2013): Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, paragraph 20. [www.wma.net](http://www.wma.net) (Accessed 22.5.2016)

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The research additionally revealed that in the case of at least three trials, foreign cancer medications were tested in Egypt despite not having approval in their country of origin. This violates the above mentioned Egyptian Regulation (127/1955). To name just a few trials: Roche tested Vemurafenib, a colectoral cancer medication that has not yet been approved in its originating country for this indication, and AbbVie sponsored a trial for cancer treatment with veliparib, a non-approved medication without a brand name so far.

### **Medicines: unaffordable, unavailable**

One way in which companies can legitimately demonstrate that they are improving the lives of the population is through affordable access to treatment after the trial is completed. According to the ethical guidelines, the benefits of research should be shared with the population where the clinical trials are carried out – this includes the right to continued treatment once the trial is over (post-trial access), and affordability of the tested product when proven successful. No evidence was found of post-trial access to treatment mechanisms put in place in Egypt. Pharmaceutical companies undertaking clinical trials in Egypt have noted that they endeavour to ensure their products are available to the population. For example, Novartis Oncology says, “We commit to registering our new treatments in every country that has participated in the clinical trials and to making the treatments commercially available wherever feasible.” However, in Egypt not all tested medicines proved to be affordable or available for the Egyptian population. The research found that in a sample of 24 medicines tested in Egypt, 9 did not receive market approval, 15 were approved, but 75% of these were not state-subsidised, making them unaffordable to the vast majority of Egyptians. For example, one cancer treatment from Novartis costs 15 times the minimum wage.

### **Company responsibilities**

While fulfilment of ethical guidelines is often included in clinical trial documents and corporate social responsibility policies of companies, the findings of the research clearly show that – in reality – companies do not adhere to the highest standards. Moreover, research also identified the violation of a specific

Egyptian regulation (mentioned above) that was established to protect Egyptians from being used as guinea pigs. Companies should act upon patients’ vulnerable status and take additional measures to protect the safety and rights of the participants, as stated in the Declaration of Helsinki and CIOMS Guidelines. However, pharmaceutical companies appear to be using the less stringent standard – Good Clinical Practice Guidelines (ICH GCP). In light of the increasing number of clinical trials involving vulnerable populations, companies should go beyond the corporately influenced ICH Guidelines and follow the Declaration of Helsinki and CIOMS Guidelines.

Pharmaceutical companies have to comply with the UN Guiding Principles on Business and Human Rights. These stipulate that companies have to respect human rights – and a breach of ethical standards should be considered a human rights violation.<sup>9</sup> Pharmaceutical companies should carry out a thorough due diligence process to identify the risks of human rights abuses. They should oversee and report on the measures taken to protect trial participants and to prevent ethical violations when they test medications in a low- and middle-income country. For ethical purposes, they should justify the inclusion of vulnerable groups, and ensure informed consent, post-trial availability of treatments, and that patients receive the best-proven treatment. Companies can and should ensure that the wider population benefits from the clinical trial. This would mean that companies then make a lasting difference in the lives of those in low- and middle-income countries and actually work towards reducing unequal access to healthcare.

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9 Fatma E. Marouf, Bryn S. Esplin (2015) : Setting a Minimum Standard of Care in Clinical Trials: Human Rights and Bioethics as Complementary Frameworks. *Health and Human Rights Journal*. no1 vol 17. 4 June. [www.hhrjournal.org](http://www.hhrjournal.org) (Accessed 11.12.2016)