

Chapter 8

Healthy Volunteers in Clinical Studies

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Abstract Patients participate in clinical trials for a variety of reasons, the first of which is often the prospect of direct health benefits for themselves. Healthy volunteers, by definition, cannot expect such benefits. In resource-limited settings, healthy volunteers are most often poor people with low literacy levels who might not understand the risks they may be taking and are in no position to refuse financial incentives. For many of them, participation in clinical trials is a critical source of income. An added complication is that some participants covertly enrol in several studies simultaneously, in order to increase their income. This exposes the volunteers to medical risks (e.g. drug-drug interactions), and also potentially biases study data. Our recommendations are that specific efforts are made to ensure proper informed consent of this vulnerable population and that compulsory national databases be established to ensure that healthy volunteers do not participate simultaneously in several studies.

Keywords Clinical trials · Healthy volunteers · Resource-limited settings
Risk · Vulnerability · National databases

Area of Risk of Exploitation

In high-income countries, healthy volunteers are sometimes university students with a good literacy level and reasonable living standards. In resource-limited settings however (including in high income countries), healthy volunteers are most often poor people with low literacy levels who may not understand the risks and are in no position to refuse financial incentives. For many of them, participation in clinical trials is a critical source of income. As a result, even though they might sign informed consent documentation, they are a highly vulnerable group that deserves

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the “specifically considered protection” recommended by the World Medical Association’s Declaration of Helsinki:

Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection (WMA 2013: art. 19).

The Problem

Informal discussions and a literature review conducted by the authors of this case study have revealed little professional interest in or attention to ethical considerations regarding healthy volunteers from low-income settings. There is very little data published on the number of clinical studies using such volunteers, making it difficult to assess the scope of the issue. While most first-in-human (phase I) clinical trials seem to be performed in high-income countries to ensure the quality of these critical studies, a very large number of studies in healthy volunteers are performed in low- and middle-income countries (LMICs) (Ravinetto 2015:3), particularly bioavailability and bioequivalence studies needed to compare originator and generic medicines.

Clinical studies using healthy volunteers are performed by international as well as local companies, often through contract research organizations (CROs). One of the few papers available on healthy volunteers in LMICs shows how CROs in India resort to “middlemen” to recruit poor participants, who have no understanding of what the studies are about and who sometimes participate in studies without informing their families. They basically “chose to participate in the trials due to insufficient income and unstable jobs” (Krishna and Prasad 2014).

Resource-poor settings are not limited to the LMICs. A few papers describe the situation of healthy volunteers in the US who have become “professional volunteers” and for whom study participation is a way to earn a living (Edelblute and Fisher 2015; Elliott and Abadie 2008). One can assume that many of the ethical issues related to US “professional volunteers” are highly relevant to their counterparts in LMICs. Many have developed tactics to conceal their involvement in several studies at the same time and have become experts at manipulating screening tests for enrolment in clinical trials, for instance by concealing their participation in concomitant studies, medical conditions, concomitant medications or substance abuse (Edelblute and Fisher 2015; Devine et al. 2013). These concealments expose the volunteers to medical risks (e.g. drug-drug interactions) and also potentially bias study data, for instance in terms of safety or pharmacokinetic profiles of the tested drugs (Elliott and Abadie 2008).

The Way Forward

We believe that specific efforts should be expanded to ensure that healthy volunteers are able to understand the key features of the studies (Phase I, II and III) they are offered to participate in, and are therefore able to provide genuine informed consent. This could be done by ensuring that documents are specifically designed for a population with low scientific literacy levels. Establishing compulsory national databases for healthy volunteers appears to be the best way to avoid some of the risks related with participation in multiple studies, detailed above (Devine et al. 2013; Resnik and McCann 2015). Some countries (e.g. France and Morocco) have set up or are in the process of setting up national healthy volunteers' databases to ensure that a given individual's involvement in clinical trials is recorded, that sufficient "wash-out periods" between trials are respected and that payments made to volunteers are tracked so as not to exceed certain levels.

Setting up national databases will require changes in countries' legislation that can only result from the mobilization of key stakeholders, including pharmaceutical companies. In addition to logistical issues that will have to be solved for such systems to be effective, ethical concerns related to confidentiality and data protection issues will have to be addressed. The EU-based pharma industry should support initiatives to ensure that this neglected, highly vulnerable population benefits from the best possible safeguards.

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Author Biographies

Klaus Michael Leisinger founder and president of the foundation Global Values Alliance, is professor of sociology at the University of Basel. He was CEO of the former Ciba Pharmaceuticals regional office in East Africa, and subsequently created and headed the company's philanthropic foundation, serving as president of the Novartis Foundation for Sustainable Development. He served UN Secretary-General Kofi Annan as special adviser on corporate responsibility issues.

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