

## Clinical trials, the State and society: where does science end and profit-making begin?

Ensayos clínicos, Estado y sociedad:  
¿dónde termina la ciencia y empieza el negocio?

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Commentary on: Ugalde A, Homedes N. Four words regarding clinical trials: Science/profit, risks/benefits. *Salud Colectiva*. 2011;7(2):135-148.

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### Introduction

Ugalde and Homedes (1) present a timely discussion of clinical trials sponsored by large multinational pharmaceutical companies in Latin America. With a forceful tone and a rare, ethically justified partiality, the authors discuss scientific frauds and manipulations of study results, financial interests disguised as science and the instrumental use of people in conditions of social vulnerability.

The arguments of these authors come together to demonstrate how preserving industrial secrecy regarding multinational clinical trials is valued more highly than the safety of the people involved. This creates a perverse logic that makes the social control of research activities difficult, thus allowing for the concealment of data manipulation and of serious events that affect research participants. Undoubtedly, this article will become one of reference regarding a fundamental issue of bioethics for Latin America and for other regions in the world, also called geopolitically "peripheral" because they are located outside the central axis of power that makes the decisions regarding the important world issues.

In this text we hope to contribute to the discussion by presenting arguments and information that reinforce the position held by the authors

of the work of reference of this debate; however, we will analyze specific aspects that to a lesser extent lend a different understanding of the analysis of the problem or a different point of view regarding possible solutions.

### A bit of history: are international clinical trials really beneficial to "peripheral" countries?

Historically, applied research was developed in close relationship with the industry, thus supporting interests and rationalities inherent to the capitalist market and gradually developing the so-called scientific-technological-industrial complex. Specifically in the health field, at the beginning of this process the possibilities of earning a profit were obviously concentrated in the development of drugs, in addition to diagnostic and surgical equipment and all other kinds of medical supplies. It was with this perspective that the complex emerged and evolved. In the present day, one hundred years after the beginning of this process, it can be asserted that clinical trials are an eminently industrial activity, and like all company initiatives they are immersed in the power games of the free market.

Thus, the production of drugs, vaccines and medical supplies was developed not as a

public concession directed at the health priorities of the population through the solid regulatory intervention of the State, but rather as any other marketable product safeguarded by property protection rules, such as the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and the respect for industrial secrecy rightly questioned by Ugalde and Homedes. In this way, all regulatory effort was focused on technical safety standards within the production that are themselves becoming increasingly weaker or, as the authors state, are simply evaded.

The eminently industrial character of clinical trials can be easily demonstrated in practice. For example, one Brazilian study discovered, using data from the national public health authority, that 95% of the clinical trials conducted in the country were sponsored by the pharmaceutical industry and the remaining 5% were split between national companies and public institutions that promote research (2). The situation is even worse when the development of the health industrial complex of a country and the research capacities of its universities are weaker. If we take into account that Brazil is currently responsible for more than 60% of the all scientific production in Latin America, we can start to get an idea of the asymmetry and gravity of this situation within our sub-continent.

At present, the multinational pharmaceutical industry is one of the most powerful economic conglomerates on the planet. The fact that the primary patents belong to only 15 companies and that the majority of clinical trials are related to the control of chronic diseases or pre-morbid states (such as diabetes, asthma, dyslipidemia and hypertension) generates a generally captive market, with business stability and continuous profitable growth. This panorama places the pharmaceutical industry in an advantageous situation in comparison with other industrial activities. The biggest pharmaceutical industries have for years invariably occupied the first places of the world ranking of industrial wealth (3). By way of example, in the year 2002 the US alone had an economic output of around 200 billion dollars in the sale of drugs (4).

Ugalde and Homedes submit as a hypothesis one aspect of the context of international research with human beings which

is already corroborated in our interpretation: most of the clinical trials carried out today are financially rather than scientifically motivated. Literature reviews regarding the drugs being developed and their indications show that multinational pharmaceutical companies orient their activities towards the same market niche, leaving aside the diseases that only affect poor or developing countries, or those rare disorders that affect just a small number of people.

In this respect, an important study published in 2006 in *Lancet* showed that of the 1,556 new drugs developed and registered by the pharmaceutical industry between 1974 and 2004, only ten were aimed at diseases found exclusively in developing countries (5). It is worth noting that it was within this same time period of approximately three decades that the expansion of clinical trials towards the "peripheral" countries occurred, which demonstrates that, contrary to the assertions of industry representatives, such internationalization cannot be considered truly "beneficial" to peripheral countries.

Other important evidence of these deviant interests is provided by studies and reports showing that in the last two or three decades companies have privileged the modification of molecules already known and commercialized with the objective of renewing for over 20 years a patent for the same therapeutic indication, or even of competing with another drug already on the market. As Quental and Salles-Filho explain, data for the year 2002 from the National Institute of Health Management (6) shows that more than half of the new drugs approved by the Food and Drugs Administration (FDA) between 1989 and 2000 were molecules already known that had undergone some type of simple modification.

Angell (4), after studying the 415 new drugs developed and registered by the FDA during the period of 1998-2002, found that only 32% involved new molecular entities and only 14% were true innovations. The author used the following criteria to define innovation: indicated for diseases that had no previous treatments available, significant superiority in relation to previous treatments, and reduction of serious adverse effects. Thus, the inflexible defense of

placebo use on the part of industry representatives, and the recent important changes made in the Declaration of Helsinki after the 51st World Medical Association General Assembly held Seoul, Korea in 2008 (7), can be understood. The so-called “methodological justifications” for the use of placebos in conditions “not threatening to human life” aim, in fact, to maximize private interests (8), allowing 70% or 80% of imitation drugs for chronic conditions or pre-morbid states to continue to be produced and commercialized.

There is abundant data that supports Ugalde and Homedes’ position regarding the small impact clinical trials promoted by the pharmaceutical industry have on the research capacity of the countries in which these trials are conducted. In this sense, it is essential to understand that the research capacity of a country is directly related to its power in determining priorities and its independence in developing projects related to these priorities. That capacity does not grow simply because private interest research studies are carried out in a particular county, whatever the quantity of studies may be. The development of research capacity depends on *national programs* that specifically include – in addition to the the natural private interests of the industry – public interests. At the same time, these programs must stimulate the capacity to transfer new technologies and practices to local groups of researchers committed to the public health priorities of their countries, so as to contribute to the research independence of the local scientific community and to society’s power to regulate and control such research.

In Brazil, according to the latest available data from the *Comissão Nacional de Ética em Pesquisa* (CONEP), approximately 79% of clinical trials protocols with foreign cooperation conducted in Brazil are phase II and III, 14% are phase IV and only 7% are phase I (9). Specific data on pre-clinical studies of drugs is not available, but it is assumed that they are significantly less. This data shows that Brazil, with regards to international clinical trials, is incorporated in those phases in which the development process of a new drug had already concluded, the patent of the molecule is already registered, and what is really needed are sick

patients in which to test the drug in order to register and commercialize it in the country.

### Regarding the limitations

The few points regarding which we have a different understanding than Ugalde and Homedes are related to the way of analyzing the limitations of clinical trials and the suggestions the authors offer to strengthen the ethical assessment of protocols in Latin American countries. Regarding this first point, the authors seem to group together the methodological limitations, the limitations caused by economic interests and the limitations caused by fraud and data manipulation. Given that these problems have different origins and require different solutions, in our opinion it is necessary to address them individually.

The *methodological limitations* (such as those related to the sample size, especially when the authors state that a sample of 4,000 or 5,000 individuals is not enough to represent the variety in the population) must be seen as limitations inherent to the current level of scientific development and would even be equally problematic even if the trials were motivated by the most legitimate public health interests. The methodological limitations are those that make risk an inevitable element in carrying out a clinical trial. The solution lies in generating a national or institutional policy of training research ethics committee members in terms of better scientific education in specific methodologies and the competencies necessary to integrally assess the socio-cultural conditions of recruited populations and the characteristics of their everyday ways of life (10).

However, the *limitations caused by the economic interests of the industries*, in our opinion, exceed the power of the local committees that monitor research ethics. The authors’ suggestion that the committees become capable of determining which trials aim at true innovations and which imitations drugs respond only to the interests of the industry, in order to thus avoid their realization, seems to us incompatible with reality. It is important to make this clear, both in terms of the essential technical

requirements needed to distinguish among tested molecules and in terms of the disparity existing between the (fragile) powers of the institutional ethics committees and the (robust) powers of the international pharmaceutical industry.

The economic interests of the companies must be regulated exclusively by the State. The public health authorities of a nation must be legally empowered to prevent the participation of national institutions in trials of imitation drugs and generate agreements aimed at the development of projects that are priority for the country. The same occurs with the legal protection of a secrecy that must be broken, especially because all the molecules in phase II and III research are already patented and no rational or moral justification for such secrecy exists. Bioethicists and other members of academia concerned with this problem, as well as social movements that activate in the public health field, must stimulate this debate and put pressure on the State, exactly as Ugalde and Homedes attempt to do in this work.

Finally, the *limitations caused by fraud and data manipulation* exceed the boundaries of ethics and extend into the field of criminality. Again, the solution is not found within the committees but within the State and its legal system. Public health authorities need to be pressured by society to create technical research boards responsible for executing detailed reviews of protocols and carrying out meta-analysis of data and facts with the intention of identifying frauds and manipulation. However, it is necessary to create strict laws that strengthen the performance and the legitimacy of national systems of control and ethical review of clinical

research studies that more forcefully classify the criminality of deviant company behavior.

### Final remarks

The historical relationship demonstrated in the last decades in Latin America among the State, society and the pharmaceutical industry needs to be changed pragmatically through more adequate professional training for research ethics committee members in the region and delineated by means of new laws and regulations that are more objective, concrete and consistent.

Clinical trials were historically understood as both science and profit. That reasoning is present not only in how multinational industries are managed, but also among health professionals that carry out the studies in different areas of the world and are paid according to the number of subjects they recruit. In general, these people belong to important regional university research groups that put their names on articles already written and developed by the industry so as to be published in rigorous independent journals. The object of this criticism may also be an important professor of medicine, lavished with international trips and other expensive rewards in exchange for the influence he or she has over the prescription choices of young physicians or on the drug to be used in his or her medical department, an influence that helps to ensure the profits of the drug's sponsors.

Science itself may be an excellent ally in this struggle, as Ugalde and Homedes clearly and forcefully demonstrate in their text.

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#### CITATION

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