RESPONSIBILITIES IN RESEARCH: THE ROLES OF SPONSORS

Araştırmada Sorumluluklar: Sponsorların Rolü

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ABSTRACT

The principle of responsibility assumed special status in the contemporary scenery besides de emergence of the conception related to necessity of public control of the scientific practice. The aim of this paper was to reflect about the roles carried out by sponsors from different institutions, national and international organizations, and pharmaceutical industries when moral conflicts emerge in this context. The complexity in the daily practice of researches involving human subjects points out the obligation to enlarge the panorama of the discussion on this theme, including several social and institutional partners. In this specific case became necessary to know the potential sponsors, exceeding the question concerning to the pharmaceutical industry. The most frequent sponsors listed in the literature were: the pharmaceutical industry, specially related to international research for development of new drugs, vaccines and medical products and equipments; international organizations in the case of epidemiological studies, drugs and vaccines for neglected diseases and research strengthening capabilities; national organizations working with specific health problems of the countries or regions populations; and research and academic institutions that have their own policies for research. This paper assumes the position that an ethical conduct during the preparation, development and dissemination of a research protocol results need to be shared between different partners. However, the sponsors have a crucial role to maintain the integrity of researches, to guarantee the protection of volunteers and society at large.

Key Words: Bioethics, ethics, research, sponsors

ÖZET

Bilimsel çalışmaların kamu denetiminde yapılması gerektiği kavramının ortaya çıkmasının dışında, sorumluluk ilkesinin de çağdaş bilimsel yaklaşım içinde özel bir durum taşıdığı kabul edilmektedir. Bu yazıda, ahlaki çatışmalar ortaya çıktığında farklı kurumlar, ulusal ve uluslararası kuruluşlar ve ilaç endüstrisinden sponsorlarca bu bağlamda yerine getirilen rollerin yansıtılması amaçlanmıştır. Denek olarak insanların kullanıldığı araştırmaların karmaşıklığı nedeniyle, bu konudaki tartışmaların bazı sosyal ve endüstriel paydaşları da kapsayacak şekilde genişletilmesi zorunluluğu ortaya çıkmıştır.

Bu özel durum farmasötik endüstriyi ilgilendiren problemlerin dışında yer alabilecek olası sponsorları tanımlama ihtiyacını doğurmuştur. Literatürde en çok adı geçen sponsorlar; özellikle yeni ilaçlar, aşılar ve tıbbi ürün ve ekipmanlar geliştirmek için uluslararası araştırmalar yürüten farmasötik endüstrisi; epidemiyolojik çalışmalar ile ihmal edilmiş hastalıklar için ilaç ve aşı geliştirmeye yönelik çalışmalar yapan uluslararası organizasyonlar; bölgesel ve ulusal düzeyde özel sağlık problemleri konusunda çalışan ulusal organizasyonlar ve araştırma alanında kendi politikalarına göre çalışmalar yapan araştırma ve akademi enstitüleridir. Bu derlemede, araştırma protokol sonuçlarının hazırlık, çalışma ve dağıtım basamaklarındaki etik sorumluluğun farklı paydaşlar arasında paylaşılması gerektiği varsayılmaktadır. Bununla beraber, sponsorlar yürütülen çalışmaların bütünlüğünün sağlanmasında gönüllülerin ve daha geniş anlamda toplumun korunması açısından kritik bir role sahiptir.

Anahtar Sözcükler: Biyoetik, etik, araştırma, sponsor

INTRODUCTION

The globalization of health research process rises questioning especially concerning to the economical aspects and partnerships that settle down for the development of studies. Unequal relationships in that context can contribute to maintain or to deepen the vulnerability of countries hosting international research, volunteers of studies and local researchers (1,2).

An international collaborative research (ICR) includes the country of origin, understood as a country in which the institution or organization that support the study are located or the country of the principal investigator's origin; as well as one or more hosting countries, those receiving the studies and where the data are collected (3).

Despite of the place in where health research is carried out, the process should be developed in compliance with a great number of national and international guidelines, as well as with existing regulation and local legislation. That scenery is complex and demands responsibility of all actors involved (4,5).

Theoretically and using a simplified definition, stakeholders are people or groups of people highly specialized in some specific topic that can affect or to be affected direct or indirectly under specific contexts (6,7). Transposing that conception to the daily scientific practice we can say that stakeholders are people and groups of people linked somehow to the process of accomplishment of researches.

Detailed analysis on that subject allows mapping the actors more commonly mentioned in ICR- such as researchers, volunteers, sponsors of the pharmaceutical industry and members of ethics committees in research- and also, those actors recently incorporated to the scenery such as policy makers, health professionals, research team, scientific editors, international organizations, media, non-governmental organizations and most important, society at large. The invigoration of the relationships among those actors will allow sharing responsibilities, to guarantee the advancement of science to enhance the future health of society, the protection of the rights and welfare of subjects under investigation and discussions related with the effective access of all population to successful products.

Traditionally, when policy makers, scientist or even society spoke about ICR, the sponsors were deeply linked to the pharmaceutical industry but in current globalized world foundations, institutions and international organizations also finance researches

and need to be considered. In the national sphere, there are different mechanisms of support for the development of investigations.

Considering all previously mentioned the aim of this paper was to reflect about the role carried out by sponsors from different institutions, national and international organizations, and pharmaceutical industries when moral conflicts emerge in this context.

HANS JONAS AND THE PRINCIPLE OF RESPONSIBILITY

The principle of responsibility assumed special status in the contemporary scenery besides de emergence of the conception related to necessity of public control of the scientific practice.

Scientific progress and technology acquired ethical importance once they began to take central position in human life. On the other hand, the proximity of the death - acted by the omnipotence of the atomic bomb and the existence of nuclear arsenals- stimulated the growth of the concern with preservation of the planet's life (8). The recently-acquired human power allowed the "creation to invade the space of the fundamental action" and as consequence the "morality has to invade the kingdom of the creation, under the form of political initiative, position that the own nature of the politics also lost temper" (9). This statement proves the tenuous limit exiting between private attitudes and public behaviours has been transposed.

The complexity of the daily situations has been demonstrated considering that science advances faster that ethics. The ethical analyses based on classical thinking could not be sufficient for the moral judgement in case of conflictive situations (10). The need to accomplish a public approach of the scientific actions demonstrates that the pluralist dimension and the diversity of focuses assume fundamental importance for the society.

The philosopher Hans Jonas proposes the adoption of the ethical imperative of responsibility, principle directed initially to the public initiative more than private conduct (11). These two spheres, although interdependent and complementary, present different facets. Private behaviours concern to people or small groups that share the same moral commitments and public behaviours emerge and they are destined to the collective. In this context, public policies formulation and implementation and elaboration of proper legislation can contribute to reduce the inequalities exiting in the society.

Considering these issues, the ethics of responsibility should take into account as a strategy for a long period, looking at the future and as one of the alternatives capable to guarantee an inhabitable world for the future generations (11). Its practical applicability takes in account the maintenance of the dignity and human integrity, since the human being became the object of technology developed in the domains of biology and medicine.

The ethics of responsibility as part of the daily activities in the context of health attention and scientific practice - including the development of experiments with human beings-should be a mandatory because in this context the ethical neutrality is an unacceptable posture. The ethics of responsibility approaches itself to the ethics of solidarity, which represents the opportunity of "to be with" and "to put in the place of" with the objective of proposing justice for the global society (12,13).

Those principles are especially applied to researches involving human beings. It is not an easy mission considering the research process, which includes conception, design, ethical revision, technology transference and socialization of the results (4). The assurance that the volunteers won't be exposed to abusive situations and additional risks needs special and constant consideration and surveillance. The researches' development contributes to the knowledge production -that can be diffused and incorporate to the process of health

attention-, but each participant should be considered and protected of potential risks and exploration (5).

The discussion about the use of a small portion of the population on behalf of the benefit that can occur for the society needs to be better evaluated. The responsibility for the protection of voluntaries' dignity crosses the private sphere of the relationship researcher-participant of the studies. It is inserted in the public sphere and it requests the compromising of the stakeholders, with special attention for the sponsors of the studies.

WHO ARE THE SPONSORS?

Detailed analysis of this question points out the diversity existing in this context. Table 1 systemizes the most important sponsors indicated in scientific literature.

Sponsors are key stakeholders for the following reasons: they provide financial resources for the project; in some cases assume the responsibility for the project design, work with the management team, select the research teams, provide scope clarification, and monitoring progress during the conduction of the

Table 1. Most important sponsors, kind of researches developed by each one of them, and expected products.

Sponsors	Kind of researches	Expected products
1. Pharmaceutical companies	Collaborative international research Clinical research	• New drugs • Vaccines • Diagnosis kits • Medical products • Medical equipments
2. International organizations • Governmental departments • Agencies • Foundations • International institutes • Universities • NGOs	International collaborative agenda Epidemiological or social studies Observational and longitudinal studies Specific subjects of interests	• New drugs and vaccines for neglected diseases • Diagnosis kits • Data for agenda policies • Evidence to design international policies for health care and health educational programs • Strengthen research capability (good clinical and ethical practices) • Creation and expansion of bio-banks and databases • Strengthen partnerships • Production of educational materials • Research networks
3. National organizations • Governmental departments • Agencies • Institutions • State Foundations	National collaborative research and Specific subjects of interests Evaluative researches	• Drugs, vaccines and diagnosis kits • Stem cells researches • Evidence to design and restructure public health policies • Evidence to design and restructure educational health programs • Definition of training programs • Research networks • Evaluation of programs and health care delivery
4. Educational institutions	Epidemiological, observational and social research Pre-clinical and clinical research Specific subjects of interests	• Strengthen partnerships between institutions from different regions in the country • Strengthen research capability • Production of educational programs • Training programs for young scientists • Increase the number of publications from staff and students of institutions

research. Under specific situations there are more than one sponsor for the project depending on its importance and extension (14).

In clinical research field, traditionally linked to pharmaceutical companies (15), the sponsor is defined as "an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial" (16). Usually the principal investigator assumes the project management or be a part of research team. In both cases he/her is formally linked to the company and contributes to the project's success.

At international level, sponsors are represented by institutions and their respective grants and funding opportunities programs, governmental departments, foundations, research institutes, universities and nongovernmental organizations (17-21). The most important objective of researches development is to produce generable knowledge for better understanding of human biology, to contribute for modify the epidemiological profile of populations, to improve access to health care, and to solve the major health problems in an unequal world. In this context, sponsors assume the commitment to interact with other key stakeholders and partnerships should consider the balance entre different aspects such as knowledge production, population's health priorities, possibilities of technology transfer, and strengthening capabilities of research institutions and investigators.

At national level, principal sponsors are governmental departments, organizations, agencies and state foundations. For this group of sponsors we will take as example the Brazilian case (22-26). Calls for applications are public, very well disseminated and research groups or individual investigators can submit proposals to apply for grants and funding. There are, at least, four types of call for applications:

1. Spontaneous: The investigators or research groups submit protocols related to their subjects of interest, there are no limits for themes and methodologies;

2. Induced: The sponsor defines the subject of research after public consultation, definition of research priorities or analysis of the epidemiological profile of the region;

3. Research by invitation: The sponsor invites consolidated and experienced research groups to coordinate national researches about special issues of interest for public health; and

4. Research plus training program: Directed for individuals: Undergraduate and graduate students, young scientists; scientists.

Another initiative was the establishment of research networks as the following examples: 1. the National Clinical Research Network in University Hospitals with the objective to offer a Brazilian response of international dependency of drugs development (27); and 2. National Cellular Therapy Network (RNTC) constituted by eight Cellular Technology Centers and 52 laboratories specially selected for this network (28).

The research protocol approved by the financing agency only receives the grant resources after its submission, review and approval by a research ethics committee (REC) or the national commission of ethics in research (CONEP) (29).

Universities and educational institutions define their own research priorities agenda considering the national scene and the institutional policies to support researches and educational agenda. However, the social responsibility of universities has grown since the institutions agreed to allocate the grant's resources. The notion that connects higher education to society at large points out the responsibilities that have to be assumed by administrators and staff personnel (30).

The complexity that emerges from this scenery is critical for sponsors, especially in collaborative research. Besides the technical and ethical responsibilities, they have to ensure the lack of financial or other conflicts of interest between sponsor institution and investigators.

Table 2. Sponsors and expected responsibilities

Sponsors	Expected responsibilities
All sponsors	• To respect the international and local ethical guidelines, regulatory aspects and specific legislation related to research involving human beings; • To submit the research protocol for a pre-review and approval by a Research Ethics Committee (REC) located in the place where the study will be conducted besides the approval in the sponsor's country*; • Beginning the data collection only after the approval of the protocol by a REC; • To make sure that study could be conducted in accordance with the approved protocol; • Sending to REC every modification in the approved protocol; • To guarantee the protection of voluntaries included in the study and the integrity of the research; • To be certified that the research has scientific relevance for the involved community; • To respect the ethical accompaniment of the study indicated by the REC; • To clarify and minimize economical and other conflicts of interest.
Pharmaceutical industry and international organizations (specially in researches with drugs, vaccines, and treatments)	• To design the research protocol and present the detailed plans of action and procedures to conduct the research; • To register the clinical trial in searchable database • To select qualified research team to conduct the research protocol; • To certify of the appropriate ethical review and approval of the protocol by a REC in both countries: sponsor's and research team's countries; • To assume the costs for the development of the study; • To be responsible for the integral assistance of the participants in case of complications related to the research protocol; • To present in the protocol the insurance policy for indemnity cases; • To assume the co-responsibility to guarantee the respect and rights of the participants; • To send the research team and the REC the modifications and amendments in the approved protocol; • To make sure about the relevance of the research for the volunteers and community involved; • To supervise the implementation of the research; • To promote the research integrity, including the accuracy and protection of the collected data; • To assure the devolution of the results to the scientific community, the involved community and volunteers; • To disseminate widely the results both positive or negative; • To assure the access of benefits and products resulting from de research development; • To improve the quality of healthcare offered to de local population; • To contribute to build the capacity and independence of local researchers.
Governmental organizations	• To define the research issues in accordance with the health research agenda of the country; • To verify the scientific and ethical relevance of the submitted proposals to call for applications; • To analyze if the proposals can answer the health needs for specific or bigger groups of the population; • To analyze if the expected results could be incorporated to public health policies and educational health programs.
Research and academic institutions	• To establish specific policies to promote the development of research involving human beings (and animals too); • To make available financial support and resources for researches development; • To elaborate guidelines and proceedings to evaluate and minimize the occurrence of improper conduct and conflicts of interest in research; • To analyze if the dissemination of the results – communications in congress and published articles – are trustworthy; • To promote the creation and consolidation of RECs, that can act independently to perform the initial review and the ethical supervision of the research; • To provide the necessary infrastructure for the functioning of the REC; • To follow the elaboration of criteria for election of REC's members; • To follow the activities developed by the REC; • To promote the educational programs on Ethics in Research for REC's members, researchers, young scientists, students and society at large.

* Local Research Ethics Committee could be understood as a committee linked to a national authority in the country or a research institution in the city where the protocol will be conducted.

SPONSOR'S RESPONSIBILITIES

International ethical guidelines for biomedical research involving human subjects are accepted as standards on adequate practices for health, epidemiological and social researches (16, 31-38). In spite of this, key stakeholders' responsibilities have not been addressed in a systematic way, with the exception for sponsors from pharmaceutical companies. Table 2 presents a list of sponsor's responsibilities which was elaborated taking as reference the international guidelines/documents and the scientific literature.

Independent of the origin of funding and type of research that will be developed, the sponsor is responsible to respect scientific and operational aspects. Ensuring studies integrity reinforces the indissoluble link between scientific design and ethical requirements (39, 40). Stakeholders' commitment to conduct studies in agreement with highest ethical standards aiming to guarantee the respect for participants' rights and reinforce principles of equity, responsibility and respect (41).

Clinical trials incite a lot of ethical questions considering the consequences of direct intervention on the volunteer's body and their submission to potential risks. The development of biomedical research in developing countries has achieved extensive visibility since the publication of results of studies considered ethically questionable. Researches using African and Southeast Asian women to investigate the effectiveness of a short intervention to reduce vertical transmission of HIV, including the use of placebo for the control group, exposing the vulnerability that are submitted the populations of those countries (42,43).

After the publication of the results, the world-wide reaction was immediate becoming mandatory the discussion about the necessity to be attempt to increased flexibilization of ethical criteria depending of the place and local standard of care where the research was conducted. It became evident that the possibility to eliminate, or at least minimize, the exploitation and abuses of vulnerable people and communities in low income countries started to be a responsibility of scientific and lay global communities. In addition, more attention was directed to the disclosure of economical or other conflicts of interests related to the conduction of researches.

No less attention needs to be directed to social research in health. The ethical responsibility starts with the required respect for actors' inter-subjectivity, including volunteers, researchers and community members. Special aspects related to the use of concept of minimal risk, protection of privacy and confidentiality and informed consent process, associate methodological and ethical issues aiming to avoid abuse of power. Therefore, the relationship between sponsors, principal investigator and research ethics committees needs to be very close to increase awareness of the potential benefits of this approach and contribute to comprehend different facets of human health and approach behaviors adopted by individuals or groups of people (44, 45).

After careful analysis of the context where the research will be conducted, other responsibilities could arise and incorporated by sponsors and key stakeholders. The personal and collective commitment represents a green signal to guarantee the protection of volunteers, researches, institutions and society at large.

CONCLUDING REMARKS

This argumentative paper assumes the position that an ethical conduct during the preparation, development and dissemination of a research protocol results need to be shared between different partners. However, the sponsors are key stakeholders and assume a crucial role to maintain the research integrity, what guarantees the protection of human volunteers and society at large.

To share responsibilities imply the act of working together to develop an ethical culture, based on the

human rights statement, to be effectively incorporated to the scientific practice. The scientific design of the study must be accompanied by the acceptance and implementation of ethical requirements during the different phases of the research development.

Some benefits arise from this approach. Through the lens of ethical analysis, sharing responsibilities requires a plentiful dialog between key stakeholders and society. In a pluralistic world, the moral conflicts represent opportunities to argue out sensitive issues including new players in the debate. The international and national guidelines for health research are only the beginning of the discussion. It is necessary to make a critical exercise to scrutinize the existing gaps related to responsibilities required in this context. The benefits are evident: it will be possible to specify the person or groups, as well as their duties, in the research development process.

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