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## Health Universal Access and Innovation: the Triple Helix Approach in Action

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### Abstract

This paper presents how innovation in health/health services in IDCs - Innovative Developing Countries (developing countries with relevant investments in education, health research infrastructure, and manufacturing capacity in the last decades) can benefit from the Triple Helix approach. Diseases affect populations of developed and developing countries unequally in terms of disease burden distribution worldwide and in the R&D investment in health. Global diseases are object of intense R&D, whilst diseases related to poverty (or neglected diseases) do not receive the same attention from pharmaceutical industry. This market failure scenario highlights the role of the IDCs in the struggle against neglected diseases, since they are closer to the reality of such diseases and have an increasingly capacity to cope with health issues globally. In this sense, the case here presented is an example of the potential offered by Triple Helix approach to address the neglected diseases issue. Despite technology transfer agreements being a widespread practice of Brazilian Ministry of Health, when it comes to neglected diseases, its effectiveness is limited, due to the market failure already mentioned. Nevertheless, in an IDC environment the Ministry of Health can make use of its purchasing power both to introduce a new product in the Unified Health System, ensuring the nationalization of production, and to stimulate private investment in R&D for neglected diseases. The mechanism used in this case: the association of technology transfer to collaborative development of a new product, presents itself as a feasible option to foster innovation in neglected diseases, combining the efforts of a private company, a public R&D institution and an innovation policy with a strong presence of the Ministry of Health and respective use of State's purchasing power. We argue that the feasibility of such an action depends on the presence of two key elements: Brazil's condition as an IDC and the articulation of these three key actors as proposed by the Triple Helix Approach.

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## 1. Introduction

This paper presents how innovation in health/health services in IDCs - Innovative Developing Countries can benefit from the Triple Helix approach. Diseases affect populations of developed and developing countries unequally in terms of disease burden distribution worldwide and in the R&D investment in health. Global diseases are object of intense R&D for new drugs, vaccines and diagnostic tests. Diseases related to poverty (or neglected diseases) do not receive the same attention from pharmaceutical industry, since they are endemic only in poor countries and potential returns on investment are low if compared to the possibilities of products directed to global diseases.

This market failure scenario highlights the role of the IDCs in the struggle against neglected diseases, since they are closer to the reality of such diseases and have an increasingly capacity to cope with health issues globally. In this sense, the case here presented is an example of the potential offered by Triple Helix approach to address the neglected diseases issue.

Brazilian State provides universal access to health for all citizens. Public health actions and services are part of an organized network, which is also responsible for scientific and technological development. In this context, Ministry of Health plays a central role in political actions related to science, technology, innovation in health, and technology transfer partnerships between public sector R&D institutions and private pharmaceutical companies.

Despite technology transfer agreements being a widespread practice of Brazilian Ministry of Health, when it comes to neglected diseases, its effectiveness is limited, due to the market failure already mentioned. Nevertheless, in an IDC environment the Ministry of Health can make use of its purchasing power both to introduce a new product in the Unified Health System, ensuring the nationalization of production, and to stimulate private investment in R&D for neglected diseases.

This is the case of the partnership between Fiocruz and GlaxoSmithKline Biologicals S.A (GSK), one of the world's leading research-based pharmaceutical companies dedicated to vaccines. In August 2009 both institutions started a partnership directed to transfer the GSK technology of pneumococcal vaccine to Fiocruz, and to start the collaborative development of a vaccine against dengue fever (with possible inclusion of R&D on malaria and yellow fever vaccines). The mechanism consists of linking a collaborative agreement to develop a new product (for a neglected disease) to an agreement designed for technology transfer (global disease).

The paper starts by showing the recent trajectory of the current legal and institutional framework for innovation in health in Brazil, with emphasis in the public sector, and then presents de case study of the partnership between Fiocruz and GlaxoSmithKline. In the sequence, findings and interpretations of the case are discussed. In the conclusion it is showed how innovation in health/health services can benefit from the Triple Helix approach, and implications for policy making in developing countries are made.

## 2. From basic research to a Triple Helix approach in health policies: the crafting of the legal and institutional framework

This paper presents how innovation in health/health services in IDCs - Innovative Developing Countries can benefit from the Triple Helix approach. Brazilian Federal Constitution of 1988 states that every Brazilian citizen has right to public health care. Therefore it is a duty of the State to guarantee such right through social and economic policies directed to provide universal and equal access to health actions and services, and to reduce the risk of disease.

Historically, health has always occupied a prominent place on the research activities carried out in Brazil, being the public institutes dedicated to health research among the most important scientific institutions in the country since the nineteenth century [1]. In the early twentieth century, Oswaldo Cruz Institute in Rio de Janeiro, and Butantan Institute in Sao Paulo, were prominent in health research in the national scene, even before a formal university research system emerged in the 1930s [2]. Yet, despite the high standards of scientific health investigation performed in Brazil, there has always been an evident discrepancy between the hegemonic core of health research and health policies, which resulted in a widening gap between the subject of research and the health needs of the population [1]. Thus, despite the scientific capabilities, the country's capacity to innovate in health goods such as medicines, vaccines and diagnostic tools remained limited.

A movement towards connecting the policy of science and technology with the health needs of the population only occurred when both the development model based on import substitution and the neoliberal pattern that succeeded it, failed to meet the new challenges placed on the international scenario to cope with emerging or reemerging diseases such as HIV/AIDS and tuberculosis. This health sectoral reaction triggered a series of initiatives that resulted in 1994 in the First National Conference on Science and Technology in Health, when for the first time in Brazilian history, a proposal for an explicit and comprehensive National Policy on Science and Technology in Health was drawn up, but most of its resolutions were never implemented [3].

Given the failure of the initiatives proposed in the 1990s, in the middle of the next decade, the country launched a series of initiatives aiming at consolidating a national system of innovation, through successive public policies and the reformulation of its regulatory framework, seeking to strengthen science and its potential for innovation, particularly through the encouragement of private sector investment and articulation of various actors (public and private) in the innovation system [2]. Examples of these initiatives are the Laws of Innovation (Federal Law No. 10,973/2004) and Tax Incentives (Federal Law No. 11.196/2005, known as "Good Law"). The first one intends to strengthen the R&D present in the relationship between research institute and industry, in a clear Triple Helix approach, and the second deals with a vast framework of tax incentives, including those to promote innovation.

Under these circumstances, and among various strategies employed by the Ministry of Health to promote technological innovation, it is remarkable the use of its purchasing power and an upgrade in technology transfer agreements, such as the partnership to develop an inactivated vaccine against dengue between the Oswaldo Cruz Foundation and GlaxoSmithKline Biologicals, here presented.

### 3. The case

The Oswaldo Cruz Foundation started its partnership relation with GlaxoSmithKline in 1985 and, since then, nationalized the production of vaccines for public health priorities in Brazil including polio, *Haemophilus influenzae* type b (Hib), measles, mumps, rubella and rotavirus [4]. Another step was taken on August 17, 2009, when both engaged efforts to transfer technology of pneumococcal vaccine manufacture and to jointly develop a vaccine against Dengue. The partnership between the company and the Foundation enabled the integration of the product in the National Immunization Program in 2010, and the vaccine, whose each dose can be marketed at a US\$ 32.00 price in the international market, is now freely available to the Brazilian population [6].

The agreement establishes the gradual technology transfer to Fiocruz, until it is fully able to manufacture the product. It is estimated that this process will take 10 years to be completed [7]. At first, Bio-Manguinhos will make the final stages of production and quality control of the vaccine, advancing gradually to a full transfer of technology, when the product will be fully manufactured in Brazil [8]. The partnership states the annual supply of

approximately 13 million doses of vaccine, enough to cover the 3,2 million children born every year in Brazil. The Ministry of Health estimates to invest R\$ 400 million per year to purchase the pneumococcal vaccine [9].

As it has already been mentioned, this is not the first production technology transfer carried out in Brazil, and it would be just another one despite the fact that, along with the partnership to transfer the production technology of the pneumococcal vaccine, Oswaldo Cruz Foundation and GlaxoSmithKline have agreed to join efforts in research and development of new products. This fact turns just another production technology transfer contract into a rather relevant case for study and disclosure of comprehensive inputs for policy implications.

Also relevant here is to understand the reasons why Fiocruz's participation is important, and why this agreement has only been possible in the present macro scenario, which will be done later. Back into the case data, in this collaborative research and development agreement, the parties cooperate to develop a vaccine against dengue, with company's investment of EUR 35 million in return for the participation of Fiocruz [9]. The agreement also anticipates the possibility of join efforts for the development of two vaccines against other neglected diseases: yellow fever and malaria [7].

The intent is to develop an inactivated vaccine for dengue, based on the success of Japanese encephalitis inactivated vaccine developed by GlaxoSmithKline. The vaccine platform technology to be developed uses high density cell culture technology in the production of viral antigens. This platform can also be used for development of other inactivated viral products, such as the vaccine against yellow fever and polio. Under the terms of the agreement, the patent results will be shared by the parties [7].

The development schedule is also estimated in 10 years, starting from 2009. In the early years, the parties shall cooperate in process development, pre-clinical evaluation and production of materials. In that way, the first evaluation results of the inactivated vaccine should be obtained after five years of research [7]. During the preclinical phase studies animal models will be used for proof of principle and safety assessment for clinical trials, when the product will be finally tested in humans [8].

To achieve the objective set, the agreement includes interchange of scientists and technicians of the parties and the collaborative work of such professionals in the research program. The activities are directed by a steering committee composed of representatives from Fiocruz and GlaxoSmithKline [7]. This initiative contributes to strengthen scientific and technological capacity of Fiocruz, presenting the possibility of new collaborations to develop vaccines with a similar approach [8].

The technology transfer component of the partnership described above follows the structure of previous agreements between the Fiocruz and GlaxoSmithKline. The same occurs in other agreements of the Foundation to absorb the production technology of biopharmaceuticals and diagnostic kits, as well as in partnerships of other Brazilian public laboratories with multinational pharmaceutical companies for technology transfer of products of interest to the Ministry of Health. The novelty here presented relates to the component of R&D of new products.

In this sense, it is noteworthy that not only the R&D agreement provides, in an unprecedented way, the collaborative development of new products between a public institute of R&D and production and a multinational pharmaceutical company, but also enabled investment in neglected diseases. To realize the importance of the arrangement one must take into account the notorious difficulties related to attracting the big pharma investments on neglected diseases. According to Mary Moran, the motivation of these companies to invest in such diseases assumes some particular characteristics:

*Big companies involved in neglected-disease R&D were not motivated by commercial returns in the neglected-disease market, but rather by longerterm*

*business considerations, including: (1) minimising the risk to their reputation stemming from growing public pressure on companies over their failure to address developing country needs; (2) corporate social responsibility and ethical concerns; and (3) strategic considerations (for example, positioning themselves in emerging developing country markets, or building access to low-cost, high-skilled developing country researchers) [10].*

The novelty described above suggests that the partnership between Fiocruz and GlaxoSmithKline has characteristics that distinguishes it from other typical arrangements for product development. In the next session, some possible interpretations of the reasons why this agreement has been made possible are discussed.

#### **4. Findings and Interpretations**

The interpretations here presented are divided in some specific topics, related to: (i) Brazil being an IDC country; (ii) the legal and institutional framework that has been crafted throughout the years to meet the needs and priority setting of the country, specially in what relates to health issues, as described previously; (iii) the use of the State purchasing power, and finally (iv) the importance of building trust and cultural aspects for fostering agreement between public and private institutions.

It is important to mention that, although none of the arguments presented may explain alone the novelty of the agreement between Fiocruz and GlaxoSmithKline, and also justify the presence of this paper in a Triple Helix Conference, the summing up of them turns it clear that these are rather relevant aspects to consider when thinking the TH approach to foster development and innovation in so-called developing countries.

One of the hypothesis presented for the effectiveness of this attempt, that has been crafted together with the crafting of the institutional and legal framework presented in the previous section, is the special condition of Brazil as an *innovative developing country*, since this condition allows the country to meet a number of circumstances that enable the collaborative development of products aimed at combating neglected diseases.

According to Morel and colleagues [11], the Innovative Developing Countries are developing countries more scientifically advanced than others, which can undertake higher degrees of health innovation, reaping the benefits from decades of investments in education, health research infrastructure, and manufacturing capacity. Despite not having advanced economies to the point of being considered developed countries, IDCs such as Brazil, China, India, Argentina, Chile and South Africa have considerable indigenous capacity in science and technology and are able to discover, develop, manufacture, ensure safety, and market new health products.

To be more explicit, only a developing country with characteristics of an IDC (which means that not every developing country is an IDC) could create and host a public R&D institution like Fiocruz in its territory. The Foundation is a world major public health research institution and has a unique organizational configuration to integrate a range of activities which include research and development, hospital and ambulatory care services, production of vaccines, drugs, reagents, and diagnostic kits, education and training of human resources, information and communication in the area of health, science and technology, quality control of products and services, and the implementation of social programs. The institution has a long tradition in research on tropical diseases and has several projects to develop new vaccines in its portfolio, such as another dengue vaccine through an alternative technological approach [7], a new generation of vaccines against yellow fever and malaria based on recombinant DNA technology, with patent filed and issued in Brazil and abroad [12].

It is therefore clear that this IDC condition turns it possible to bring together capabilities from both sides (Fiocruz and GlaxoSmithKline) to enable the joint development of a new product, sharing risks and increasing speed and the prospects of success. Both Fiocruz and GlaxoSmithKline have renowned and complementary expertise in R&D in the area and hold intellectual property relating to the object of collaboration, making it mutually advantageous the joint efforts for product development. Without the scientific and technological capacity of Fiocruz, plus the intellectual property the institution holds, it would be virtually impossible to attract a multinational pharmaceutical company to a collaborative development project, in partnership with a public laboratory in a developing country with such a degree of results sharing.

In this context, is relevant the likely influence of the long history of partnerships between the two institutions, which provides greater security to negotiate sensitive issues for the organizations such as patent sharing and exchange of scientists and technicians. If there were no mutual trust between the parties, it would not be possible to establish a collaborative development program, since the implementation of joint R&D implies the mutual disclosure of confidential and strategic information.

This specific question is stated in this session, since it is important to mention the role building trust plays in the effectiveness of innovation initiatives and contracts between public and private sectors, specially in countries where these actors have traditionally seen each other as *quasi* opponents (it is assumed that this is the case in many developing countries).

Concerning this trust/security aspect, it is relevant to come back to the legal and institutional framework, which is responsible not only for creating and sustaining the environment where such partnerships integrating government, public R&D institutions and private sector may occur, but also for accompanying international trends and rules. In this specific case, as for sharing confidential information and patents, it is important to remember that there is a system of intellectual property protection structured in Brazil according to international standards set out in the TRIPS agreement. In this sense, it is worth noting that intellectual property protection is considered a critical factor for the pharmaceutical industry for contracting business involving technology with developing countries [4].

Thus, the legal framework relating to intellectual property is also important in enabling the transfer of technology. In this respect the Industrial Property Law (Law 9.279/96) has a decisive role as well as the Innovation Law (10.973/04), which includes the legal provision of technology transfer within the scientific and technological institutions (such as Fiocruz) legitimizing the existing practices in public laboratories. Therefore, the Innovation Law brings the legal basis to support such specific contracts, providing greater legal certainty to the agreements in the spirit of Brazil's innovation policy.

However, its IDC condition alone does not guarantees the feasibility of agreements such as the latest partnership between Fiocruz and GlaxoSmithKline. Other partnerships involving Big Pharma, just for the development of dengue vaccine, show how unlikely it is joining north-south efforts between a multinational company and an institute devoted to R&D and production, where the parties share the results. Even when there is some participation of developing country institution, which is ubiquitous in neglected diseases product development, since clinical trials should be conducted where the disease is present, this participation is limited and the country in question does not guarantee any right on the results.

Brazil's differential with respect to promoting innovation in health is the strategic role of the Ministry of Health to foster innovation. This branch of the Federal Government is responsible for the planning and implementation of policies aimed at health promotion, prevention and attention, and also centers measures to encourage innovation in the sector. In particular, the Ministry of Health uses its purchasing power for this purpose. It is precisely the use of the purchasing power of the state that allows the formatting of arrangements for



gathering the efforts of the pharmaceutical industry and public research and production institutes for the collaborative development of products for neglected diseases, linked to a technology transfer of a product against a global disease.

In the case presented, it seems clear that the motivation that led the company to establish the collaborative development partnership with the public laboratory was not, primarily, focused on the prospects for financial returns provided by the commercial exploitation of products aimed at fighting neglected diseases. However, one cannot rule out the economic motivation provided by the agreement on technology transfer (and hence supply of products). Unescapably, the hundreds of millions of dollars to be invested by the Ministry of Health in the purchase of the vaccine against pneumococcus counterbalance the company's investments in the development of the dengue vaccine. Even if the prospect of profits from the new product plays an important role, in addition to the components highlighted by Moran (as already mentioned) [10], it is unreasonable to ignore the motivation provided by the procurement of a high added value product.

As pointed out by Gadelha & Azevedo, the use of the state's purchasing power is a crucial condition to enable the transfer of production techniques for public laboratories in Brazil. The authors explain that companies that control the technology "do not negotiate knowledge, but products", being essential the establishment of trade agreement attached to the transfer of technology, which enables the supply of products during the transfer of production knowledge phase [13]. In such a configuration, the business becomes profitable for the company which owns the technology, the public laboratory that receives it and society in general, which guarantee, respectively, the market for their products, access to production technology and provision of goods for the Unified Health System.

In this sense, Homma and colleagues add, in reference to the specific case of vaccines, that the immunizations policy of the federal government embraces the strengthening of national capacity on technological innovation, modernization and construction of new production facilities, since the use of state's purchasing power represents an important tool in technology transfer agreements, enriches national technological capacity building and ensures the supply of essential vaccines at a price compatible with the government budget [6].

In the vaccines scenario in Brazil, it is through the National Immunization Program (NIP) that the purchasing power of the Ministry of Health is used. Such program is considered one of the most complete among the developing countries and is increasing over recent years, having pioneered the introduction of rotavirus vaccine in 2007 and the pneumococcal and meningococcal serogroup C conjugate vaccines in the second semester of 2010. Homma and colleagues argue that the NIP is comparable to the immunization programs of developed countries, illustrating its robust growth in the past decade with the following figures: in 2000, the NIP's budget was R\$ 200 million and in 2009 reached R\$ 825 million, now offering 26 different types of vaccines [6].

In the example of the present case study, the use of state's purchasing power serves as an incentive not only for the nationalization of the relevant product technology related to public health, but also enables the establishment of a partnership to develop a new product. From that perspective, the structure of the partnership between Fiocruz and GlaxoSmithKline, to transfer technology and develop a new product, with the intervention of the Ministry of Health, can be used as a model to foster innovation for neglected diseases in Brazil. The mechanism consists in linking a collaborative agreement to develop a new product to an agreement to transfer technology, in a partnership involving a major pharmaceutical company and a public laboratory, with the intervention of the state entity. The object of technology transfer should be a global disease, or a product developed by the pharmaceutical company with a considerable market in the country. The object of the collaborative development must be a neglected disease.

Within the technology transfer, the company provides products and inputs to the laboratory, which in turn supplies the product to the public market. In this context, the state's purchasing power ensures the viability of the business. In parallel, through a collaborative development agreement, the company and the laboratory perform a research program, which, if successful, will result in a new product intended to fight a specific neglected disease.

From the company's point of view, the business as a whole will be advantageous to the extent that the access to the national public market compensates the investment in product development targeting a neglected disease. Such investment should be seen as compensation to the exclusivity granted to the company for its products during the technology transfer. Thus, the investment may vary depending on the market size and length of the technology transfer.

Similar variation should also be considered depending on the object of the collaborative development since the higher the potential market of the product being developed, the greater the company's investment. This occurs, for example, in the case of dengue, in which the compensation of the company was considerable, given the potential revenue in emerging markets, especially in Asia and the Americas. On the other hand, one should not require major investments, if there are no prospects for greater financial return from the commercialization of the product for a particular neglected disease. When the prospects of return are diminished, as in the case of most neglected diseases, it is natural that the public entity assumes most of the development and that the company's participation is limited to its expertise in R&D.

## **5. Conclusions and implications for policy making, in particular for developing countries**

Considering the characteristics of developing countries, and given the uncertainties inherent to the R&D activity in health/health services, where there is no guarantee of success in obtaining a new product/service, it is important that collaborative development is linked to a technology transfer. Accordingly, the model presented in the previous session offers benefits to both parts involved in the technology transfer, namely: exclusive market for the company's product during the technology transfer, the increase of the public laboratory's technological capacity and a new product to be consumed by society in general.

Analyzing Brazilian capacity for innovation, one can verify that Brazil occupies a prominent place among developing countries and could be considered an IDC. Brazil is suitable enough to occupy such position, because it has one of the most structured national innovation systems among the developing countries. Thus, the condition of IDC represents a qualitative difference for Brazil to take a leading role in developing innovations for neglected diseases.

Recent initiatives have been implemented in Brazil to create a favorable environment for innovation, especially in health, with strong presence of the public sector. The current political circumstances induce the strategic action of the Ministry of Health towards innovation. In this sense, the use of the state's purchasing power also makes the difference and can be used to encourage innovation for neglected diseases in Brazil, as illustrated by the partnership between Fiocruz and GlaxoSmithsKline. However, the use of state's purchasing power is not enough, since the establishment of a collaborative partnership for development depends on a basic R&D capacity on both sides. In this case, the joint efforts to develop the vaccine would be innocuous, if it was not for the scientific and technological Fiocruz capacity in dengue. Therefore, it is Brazil's condition as an IDC combined with its policy to encourage innovation (with a strong presence of the Ministry of Health and use of state's purchasing power), that makes the country able to contribute decisively in the development and production of new products targeted to fighting neglected diseases, in particular through the mechanism suggested.



The technology transfer component of the partnership follows the structure of previous agreements between Fiocruz and GSK and the ones between other R&D Brazilian institutions and major pharmaceutical companies. The novelty here presented relates to the component of R&D for neglected diseases, especially because it includes sharing of intellectual property rights and exchange of scientists and technicians, which contributes to strengthen Fiocruz scientific and technological capacity, opening possibilities of new collaborations for vaccine development with similar approach. Such partnership distinguishes itself from other arrangements, particularly when one takes into account the difficulties in attracting private R&D investment for neglected diseases [10] [11].

Besides the previous partnerships between Fiocruz and GSK, it must be emphasized that the particular case mentioned in this paper comprehends extra motivation from GSK, since Fiocruz has long tradition in research on tropical diseases, undertakes several projects to develop new vaccines in its portfolio and owns intellectual property related to the object of collaboration. In its turn, Brazil is restructuring its national system of innovation which now stimulates joint R&D activities and technology transfers between public and private sectors; in 1996 Brasil passed an Intellectual Property Law according to international standards under the TRIPS Agreement; and the role of the Ministry of Health to foster innovation [1] [2] [11]. Last but not least, the use of the State's purchasing power through the Ministry of Health provides extra incentive for GSK to invest in the collaborative development for a neglected disease.

Although pharmaceutical giants like GSK have extensive expertise in R&D of new products, it lacks in incentive to invest in neglected diseases since those diseases disproportionately affect people in developing countries and there is no commercial market to attract private R&D investment [10]. On the other hand, institutions like Fiocruz in an IDC environment have strong accumulated knowledge on diseases that affect their population (including neglected diseases), but have limited conditions to go through the whole process for developing a new product. In the case here presented it has been possible to bring together complementary expertise from Fiocruz and GSK to enable the joint development of a new product, sharing risks, reducing the time to be spent and increasing the prospects of success.

The mechanism used in this case to associate technology transfer to collaborative development of a new product presents itself as a feasible option to foster innovation in neglected diseases, combining the efforts of a private company, a public R&D institution and an innovation policy with a strong presence of the Ministry of Health and respective use of State's purchasing power. Coming back to Etzkowitz & Leyersdorf paper *The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university–industry–government relations* from 2000, it is clear that the attempt of countries do attain some form of Triple Helix III is present in the case study presented. Strategic alliances between firms and public R&D laboratories, encouraged, but not controlled, by government, although in this specific case Fiocruz is part of the Ministry of Health.

Noteworthy is the relevance of cultural aspects. As experienced by one of the authors of this paper, who took part in the negotiations of the contract of the agreement object of the case here presented, the past trajectory of both Fiocruz and GlaxoSmithKline and the complementary knowledge bases of them were fundamental for establishing a micro environment in which an overlay of communications and personal and professional networks could create a virtual agenda for innovative development of products. As for the government, the capacity to set new rules of the game and assure a stable ambience, besides bringing coherence to policy making in health, has also been of major importance.

In a non conclusive and non exhaustive conclusion, it is relevant to notice that the agreement here presented is hopefully the first of many other future distinct arrangements to foster innovation, considering also neglected diseases as part of the game. The dynamics of innovation, as proposed by the Triple Helix approach may assume different forms in which the actors play different roles. The openness to explore new possibilities and

configurations, assuming that this is one of the “rules of the game”, is necessary not only for countries/governments, or the State, but also for R&D institutions (be they public or private), firms and society.

The complexity of the present moment proposes a challenge for countries, universities, R&D institutions, firms and society, in which scarcity of resources is not always the case. Worse than this, and perhaps more difficult to solve, is the bad allocation of resources when there is no room left for “thinking out of the box”.

Finally, although this paper has dealt with other approaches besides the Triple Helix one, it has always had the dynamics of the helixes as a guiding star.

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