Instruments of Transformative Governance.
Product Development Partnerships for Neglected Diseases

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ABSTRACT:

Product Development Partnerships (PDPs) for neglected diseases bring different actors together aiming to provide accessible medicines for these complex diseases. Finding solutions requires advanced investments in R&D, expensive clinical trials, long medicine approval processes, and reliable drug production and distribution channels. PDPs aim at overcoming current market and government failures by pooling resources in the attempt to solve this global social challenge. Thus, PDPs are a case of instruments of transformative research and innovation, operating in a transnational governance context. They exhibit three novelties: they address strategic long-term problems in a holistic manner, set substantive output-oriented goals, and are implemented through new organizational structures. After characterizing the different types of current PDPs and the context in which they emerged, the paper examines in detail three cases of single- and multi-disease PDPs (DNDi, EVI, and MVI). The cases show that their functions have been evolving through time, as the PDPs are becoming more specialized and focused. Yet, their ability to mobilize the resources (funding, organizational, knowledge and legitimacy resources) to fulfill these functions depends largely on their capability as agents to adapt to changing opportunity structures.

1. Introduction

Neglected diseases pose serious problems for poor countries' public health and development. Providing accessible medicines for these diseases are among the most enduring and difficult grand societal challenges, as they require advanced investments in R&D, as well as expensive and long regulatory approval processes of those medicines. The low purchasing power of patients has created a market failure, limiting the investment levels from private firms. Likewise, public governments in developing countries lack the institutional capacities to develop such advanced and capital intensive R&D investments. Product development partnerships (PDPs) seek to overcome this double market and state failure by bringing together national governments, international organizations, universities, private firms and large philanthropies, in the targeted effort to find suitable ways to prevent, treat and cure these diseases. There are approximately two dozens of PDPs currently operating across borders, most of them created around the turn of the Millenium, and highly inspired by the UN Millenium Development Goals put forward in 2000. In many ways, these partnerships can be seen as a serious attempt of create new types of instruments for governing change in the complex socio-technical systems of these diseases.

The overall goal of Product development partnerships for neglected diseases is to develop affordable, effective and accessible medicines for the global poor. Generally speaking, PDPs exhibit three important novelties: They address strategic long-term problems in a holistic manner because most of them address most of the complex and expensive value chain in the introduction of new medicines (from laboratory R&D, clinical trials, and up to its introduction into the market); they set substantive output-oriented goals (virtually all PDPs have missions defined by the expected outcomes rather than by the inputs or processes as such), and they are implemented through new organizational structures created ex-novo and with new organizational arrangements.

What are PDPs a case of? Operating across national borders and across very different types of partners, product development partnerships (PDPs) are relevant examples of two new trends. Firstly, they are new types of instruments of transformative research and innovation, an overarching political agenda that sees R&I activities from a responsible angle, contributing to solve difficult societal problems. In that sense, research and innovation is conceptualized as an important mean to address complex problems, rather than a goal to promote the competitive position of individual firms, or to promote improving scientific capacity per se. For that reason, product development partnerships can be seen as instruments of transformation, rather than instruments for economic growth or for scientific development alone. At national level this is related to the raise of policy instruments to address grand societal challenges (Rogge and Reichardt 2016) (Chataway, Hanlin et al. 2014), and the growing directionality and mission-oriented nature of science technology and innovation STI policy mixes towards transformative innovation (Schot and Steinmueller 2016) (Wieczorek and Hekkert 2012).

Secondly, product development partnerships are relevant examples of transnational forms of hybrid governance, and in particular of the gradual emergence of international governance architectures, which are strategic and directional initiatives on targeted issues (Borrás and Radaelli 2011) (Abbott, Genschel et al. 2014). The peculiarity of product development partnerships is that they involve very

diverse type of actors including private actors, public actors, and civil society organizations. In that regard PDPs are very broad, combining actors with very different resources, backgrounds, goals, and capabilities. This is an example of the complexity of transnational hybrid governance. Therefore PDP's can be seen as epitomizing rapid transformations in global governance, particularly in contexts of market failure and government failure; and in context of new global governance architectures.

In spite of sharing similar goals and overall expectations, these partnerships differ significantly in their structures, funding sources, knowledge expertise, regulatory strategies, and interaction with public health authorities. Some of them include very large numbers of members, coordinating and funding a huge diversity of activities in many places of the world. Others are more restricted in terms of members and numbers of activities. Some are focus on developing vaccines in the number of diseases. Others focus on developing vaccines as well as treatment and prevention medicines in a very few diseases. This means they are very different when it comes to the diseases and the type of drugs they aim at addressing. Funding comes as well from very different sources. Some are coordinating and managing projects mainly funded from public sources. Others are mainly funded by philanthropies and private donations, acting as funding agents and managing specific projects implementing the purposes designed by those funders.

Based on governance studies and recent developments in the field of innovation policy instruments (Flanagan, Uyarra et al. 2011) (Borrás and Edquist 2013) (Rogge and Reichardt 2016), the present paper develops an approach focusing on the different functions of these PDPs. In so doing, this paper makes a contribution to the fields of transnational governance by focusing on functions in very complex and scientific dominated partnerships, and of research and innovation studies by bringing forward the analysis of a particularly relevant case of global transformative and instruments. Asking how these new instruments emerge and evolve, this paper identifies empirically the different functions they fulfill and looks at how they mobilize the available resources to fulfill them (funding, organizational, knowledge and legitimacy resources). The paper examines in detail three cases of single- and multi-disease PDPs (DNDi, EVI, and MVI). The findings show that their functions have been evolving through time, as the PDPs are becoming more specialized and focused. However, their ability to mobilize the resources to fulfill these functions (funding, organizational, knowledge and legitimacy resources) depends largely on their capability as agents to adapt to changing opportunity structures (scientific as well as institutional).

The paper proceeds as follows. The next section reviews succinctly the literature on transformative research and innovation as well as transnational hybrid governance and governance architectures. This will serve to contextualize PDPs in the broader context of changes in governance forms at the national and international levels. The section after that will be devoted to develop a functionalist approach to the study of these instruments, building further from recent approaches on the governance of socio-technical systems. Section 4 will review succinctly the nature of product development partnerships as new instruments of transformative innovation that have emerged since early 2000s in the field of neglected diseases. The paper will develop a typology of PDPs which will serve for the selection of three emblematic case studies. Section 5 will be devoted to the analysis of the three cases selected. The final section will summarize the empirical findings and distill their theoretical and analytical contribution for future studies of transformative innovation instruments addressing grand social challenges.

2. Transformative Research and Innovation and Transnational Governance.

As mentioned before, product development partnerships can be seen as new instruments of transformative research and innovation. Transformative research and innovation is an agenda that has been recently put forward by national governments and international organizations alike seeking to re-conceptualize the overall objectives of public funding into research and innovation activities. Traditionally, the ultimate goal of governmental expenditure on research and innovation have been two, namely, to expand the frontiers of human knowledge and to improve economic growth. However, with the advent of the new millennium, a third set of goals have been put forward alongside the traditional two goals. Those third goals are to provide solutions that the market and the government have not been able to achieve. In other words, research and innovation activities directed towards helping solve ground social challenges that the market nor government alone have been able to solve. This is indeed an ambitious agenda, because it is aiming to tackle very complex problems and because it aims to do so by new types of instruments that are beyond traditional private and public divide. Likewise transformative research and innovation aims at focusing on the final expected results, in an attempt to provide clear direction to the very different actors and resources involved in solving those problems. More than before, transformative research and innovation goals seek to engage very different type of factors providing collaborative forms of problem solving. This is why transformative research and innovation main instrument is essentially based on strong collaboration between public, private, and private not for profit organizations. When those initiatives are taken at a global scale, we are dealing with transformative research and innovation performed by transnational public-private partnerships. They are part and parcel of broad governance architectures. Hence, these specific instruments of transnational governance are most relevant for understanding not only how transnational governance works in practice, but also the extent to which these new instruments of transformative research and innovation will actually deliver the expected results. In order to address these matter we need to review the literature about transnational governance, paying particular attention to the state-of-the-art regarding questions about the conditions for effectiveness. In other words, and for the purpose of this paper, how instrumental are product development partnerships in terms of inducing transformative change.

There is today a very broad literature about policy instruments at the national and local levels, and about new forms of hybrid governance at the transnational and international level. From the rich literature about policy instruments we know that each instrument reveals a fairly explicit form of the interaction between the governing and the governed, and that any instrument is a condensed form of exercising social control. Therefore instruments at work are not neutral devices, they produce effects beyond and outside those effects they were programmed to provide because they structure collective action according to very specific logics, which are a local interpretation of the overall goal (Lascoumes and Le Gales 2007). To put it in plain words, instruments have a life on their own. This is why we might

expect differences in outputs and outcomes even if the overall goals and generic mechanisms are similar. Naturally, this calls for an analysis that takes into consideration the implementation of those instruments, not just their ultimate goals or organizational features.

Likewise, from the literature of transnational governance we know that most of their instruments have taken the form of partnerships. Public and private partnerships are preferred forms of instruments particularly for situations in which there is very limited statehood. Weak governmental structures and public capacities afflict many developing countries. In such circumstances partnerships between different actors seem to create mechanisms for fulfilling collective goals (Krasner and Risse 2014). In the absence of strong public institutions, it seems that public private partnerships might enhance the capacity of authority in order to address problems of the anti-commons (such as the uncontrolled use of natural resources, the impunity and no costs for polluters, and other type of negative externalities) (Pattberg 2005) (Overdevest and Zeitlin 2014), or to directly contribute to the provision of goods and services, such as public health or social security. These authors argue that several factors which determine success in that regard. Those factors are essentially legitimacy, institutionalization and capacity to address complex tasks, as well as crucial economic resources to fulfil the former. Indeed, the past evidence accumulated during the past decade or so points to support that view. Studies of transnational governance have provided important clues about the conditions for the effectiveness of these public private partnerships in transnational governance. This is the case of studies in the field of sustainable development, and related areas of collective goods in the natural environment .

Recent empirical studies about the effectiveness of transnational partnerships in the area of sustainability have provided very relevant insights. Szulecki and co-authors have tested competing hypotheses about the conditions for effectiveness of these multi-stakeholder partnerships. The authors ask whether the relative power of the actors involved in the partnerships, or the institutional design in those partnerships matter most for effectiveness (Szulecki, Pattberg et al. 2011). These two hypotheses are based on different sets of international relations theories, which put emphasis on power relations and differential strength of actors in the international scene, or those which are more leaning towards institutional accounts in terms of processes and decision-making procedures. Using a database of global partnerships in the field of sustainability, and selecting 46 cases of partnerships in the area of energy, the authors found that “the involvement of powerful actors is necessary but not sufficient for an initiatives success.” (p. 731) presence of strong countries and large firms is highly related to the number of outputs of the partnerships. However this does not explain everything. They institutionalization and internal organization structure of the partnerships is the determinant. They also find out that the activities of a partnership require different degrees of resources. Those with activities like disseminating knowledge or advocacy need fewer resources than those engaged in more complex activities. “Hence, the main policy conclusion of this article is that a partnership, in order to be effective, needs to be institutionalized, preferably in the form of an organization with an executive board that should include the representatives of major stakeholders and permanent administrative secretariat dedicated to the goal and mission of the initiative. The involvement of powerful actors can help by bringing the necessary sources and is crucial in the case of large scale partnerships established to perform difficult and costly activities.” (p. 732). These findings are highly relevant for the current focus of this paper, namely PDPs,

as most of them are institutionalized the way these authors suggests, and they are engaged in rather complex activities along the value chain of medicines' development. Yet, the different functions performed in the value chain need further consideration, particularly about what resources are most need and how are resources are put into play. Next section will explore that. In the meanwhile two crucial theoretical aspects deserve attention.

The first one has to do with what is effectiveness, and how to measure it. There is a debate about whether it is possible and desirable to analyse and measure the outputs of transnational governance, and in particular about transnational partnerships. This is related to the parallel debates about output measurement of good governance in general terms. On the one hand, there is the view that measuring good governance (in national executive branch) is important, but must not be based on narrow focusing outputs (Fukuyama 2013). On the other hand, is the view that measurement is possible and desirable to determine the quality of the executive branch, as outputs can be easily identified and measured even if they are at concrete level (Boardman 2014). These discussions need to be contextualized in the broader evaluative exercises on the role of government. Here the traditional distinction is between outputs (the specific activities that result from specific lines of action), the outcomes (which are the broader changes in behavior observable in relation to the outputs), and impact (the wider and long effects of the activities, and their ultimate contribution to problem solving) (Beisheim, Liese et al. 2014). A series of broad-based impact indicators are currently being suggested in order to determine the success of the Sustainable Development Goals target 3.3 to "end the epidemic" of neglected diseases by 2030 (Fitzpatrick and Engels 2016). It would be relevant to examine how much the advancement of PDPs have contributed to reach that ambitious goal.

The second important issue has to do with the way in which legitimacy is introduced in those theoretical discussions about effectiveness. Some authors tend to distinguish between legitimacy on the one hand as an input from a political community towards a institutionalized arrangement, and effectiveness as the final result of the activities of that institutionalized arrangement. This is David Easton's distinction between input and output legitimacy of our political system. For many decades both have been separated, in the understanding that effectiveness and legitimacy are two crucial, yet quite different aspects. With the increasing understanding of the role of output legitimacy, as well as the new called throughput legitimacy, there is an increasing view that effectiveness is highly related to popular views about the necessity and relevance of the actions in question. In theoretical terms it means that the new analytical models that seek to explain effectiveness of PPP's, are in fact introducing legitimacy as an important resource for explaining effectiveness (Beisheim, Liese et al. 2014) (Krasner and Risse 2014). In other words, effectiveness and legitimacy are highly related to each other (Kalfagianni and Pattberg 2014). This is particularly the case for areas of governance characterized by high levels of scientific and technical nature, as the effectiveness of scientific and technical solutions is highly associated to the way in which society perceives research and innovation as desirable, valuable, and trustworthy

As we have seen above, the bulk of analysis that studies the conditions for effectiveness of transnational governance arrangements, in particular public private partnerships, are in the field of environmental sustainability. Other issue areas, such as medical innovation and global health, are much less analyzed. Many of the theoretical discussions and empirical insights mentioned above are relevant but refer to

other issue areas than health. For that reason, it is important to keep in mind the differences across issue areas when defining a suitable analytical framework. Research and innovation in medical area is highly associated to a bunch of different resources such as medical knowledge, access to research equipment and devices, economic resources, as well as legitimacy issues associated with belief systems and social attitudes towards specific contents of medical research and innovation. Likewise, regulatory issues in medical research and innovation come at a two specific stages in the value chain from laboratory to final medicine. These are regulatory matters associated intellectual property rights, and to procedures and criteria of formal drug approval for market introduction. Medical research and innovation it is not only about changing the behavior or preferences of actors through specific incentives, as it is about creating procedures and mechanisms for pooling the resources of those very different actors together, coordinating their activities into one common direction. In other words, transformative medical research and innovation for solving the problem of access to medicines to global poor is about market failures, as much as it is about government failures. For that reason, it requires a broader analysis that focuses on the active allocation of specific resources. This paper suggests focusing on the different functions that product development partnerships have set up themselves to fulfil, examining how the different resources of the private, public, not-for-profit actors have been managed and organized. Next section will provide an analytical framework for doing just that.

3. Analytical framework: Functions, Resources and Capable Agents

As mentioned in previous section of this paper, product development partnerships exhibit three relevant novelties: they address strategic long-term problems in a holistic manner, they put forward concrete output oriented goals and they are implemented using new forms of governance arrangements and organizations. This paper has framed the question about how are they put in practice, how are they unfolded, developed, maintained and adapted. Previous literature has dealt with issues of effectiveness of new forms of governance in the transnational context. Building from them this paper aims at taking a step forward in that direction by identifying the functions those PDP's fulfil. It is important to examine those functions because PDP's are quite ambitious in terms of addressing the problems in a holistic way, as they look into the different steps of the complex value chain of medicine development. Generally speaking, the value chain of medicine development is divided into different clearly defined phases: scientific research at the laboratory, clinical trials phase 1, phase 2, and phase 3, the formal approval of the medicine by the relevant authorizing regulatory agencies, the management of the production process, and finally, the distribution and introduction of the medicine. This value chain takes a very long time, and involves quite different types of actors with varied competences. It is very expensive, and is highly subject to risks and uncertainty. For that reason PDPs typically focus on several functions along that value chain. Understanding those functions, the resources that are required, and the way in which those are mobilized to successfully achieve the expected outputs, is a crucial for answering the question about how PDP's are put in practice.

There are at least nine functions PDPs might address. The first one is to advocate and shape the institutional framework dealing with these diseases or group of diseases. This is done through awareness rising, regulatory advocacy, or communicative strategies. The second function has to do with the promotion and financial support of specific R and D activities conducted by other organizations. This has to do mainly with managing funding, coordination of other actors' activities. A third function is to conduct in-house research, using facilities owned or controlled entirely by the PDP. This is the traditional engagement with research and scientific activities, through carrying on specific research projects and controlling completely the outcomes of scientific research. The fourth function is to conduct development activities, most importantly clinical trials. Clinical trials in phase 1 are about translational research, putting the scientific results from the laboratory into the context of specific medical solutions; clinical trials phase 2 and phase 3 are about testing those results into real medicine development. Clinical trials are regulated by very specific procedures and scientific methods that are key for an eventual approval of the medicine for human treatment. The fifth function is to integrate research and development knowledge from other research and innovation organizations into the work of the PDP for developing and testing new medicines. This is particularly important in the clinical trials phase, as the results from other scientific activities than those controlled or financially supported by the PDP might be essential. Typically new medicines are not just the outcome of one single result from the laboratory, but the result from many different scientific and research efforts. Those efforts and results might not be easily accessible, or freely available, for the PDP. Therefore the function of integrating previous scientific knowledge and negotiating the terms of that is fundamental for the advancement of the purpose of the PDP. The sixth function of any PDP is to secure access and affordability of the newly produced medicine. This requires negotiation and guidance of the process of production and distribution, as these involves not least very important questions of ownership and costs. Whereas issues associated to intellectual property rights are relevant in all the steps mentioned before, it is in this function that those become most crucial. Cheap and accessible medicines are the ultimate goal of PDPs, for that reason it is paramount that costs of production and distribution are kept to a minimum, while complying fully with international safety standards. These new drugs must fulfil the same high standards as any other conventional medicine production. The seventh function is to assist the introduction of the new drug into the health systems. This does not come automatically as health professionals must become aware of the new medicine, and it might require some changes in existing practices surrounding the use of the new medicine. When the new medicine is a vaccine, the introduction into the health system might require a specific vaccination program. Coordination and collaboration with local health authorities is paramount. The eighth function is to provide knowledge and expertise in processes of harmonization of regulatory or quasi-regulatory frameworks. The complex nature of the social, economic, health systems related to these diseases require often times regulatory or quasi-regulatory frameworks that that are conducive to a homogeneous governmental approach. It is PDP's might act as knowledge experts helping to create needs more homogeneous and effective regulatory frameworks. Last but not least, the ninth function has to do with building capacity in the countries afflicted by these neglected diseases. Oftentimes the PDP's aim at co-creating solutions with the organizations and stakeholders in developing countries. This co-creation can only take place if those stakeholders have the necessary knowledge and economic resources to make that happen. For that reason, one of the most important functions of PDP's is to build up such capacity in order to make co-creation happen.

Box 1: The nine functions of PDPs

1. Advocate & shape institutional framework (communicative, awareness raising, regulatory advocacy) on the specific disease
2. Promote & support (financially, and knowledge) specific R&D activities conducted by others
3. Conduct in-house novel research
4. Conduct development & clinical trials
5. Integrate research and development knowledge from other R&I organizations
6. To negotiate and guide key aspects of the process (putting clear requirements on IP, openness of knowledge, etc) in order to secure access and affordability
7. Assist implementation of drug introduction into the health systems.
8. Provide knowledge and expertise in processes of harmonizing regulatory frameworks
9. Build-up capacity in health R&D (clinical trial sites, translational medicine units, etc) in countries affected by the diseases.

As can be seen above, those seven functions are very different in nature. They are all important in PDP holistic view of the value chain in medicine development, and the attempt to provide solutions from beginning to end. Yet, these functions require a great diversity of resources. Being able to command them into a successful output is the main task for successful PDP implementation. PDPs are equipped with very different resources, four of which seem to be key: economic funding resources, organizational and management resources, scientific and technical knowledge resources, and legitimacy resources. Economic funding resources refer to the budgets that are both given from partners and donors. Those contributions might be in-kind or monetary, the later subsequently used or distributed to implement the actions defined. Most often PDPs do that through individual projects. Some projects are long and expensive, broad and ambitious. But in most cases projects are specific time-limited and rather concrete in their goals. Organizational and management resources are the second type most crucial for fulfilling the functions described above. PDP's are very complex partnerships, involving partners, wider stakeholders, and final users. PDP's are accountable to those, for that reason organizational and management resources are key to implement and come to positive fruition the efforts of those involved. Scientific and technical knowledge resources, are another type of vital resources in the field of medical research and innovation. The nature of the scientific challenge is very high, and it goes the same for the medical challenge. The complexity of the diseases at hand is very high, and no easy solutions are yet been reached. This is combined with the challenges associated with the delivery and practice of medicine in less-developed countries, which encounters many obstacles. Knowledge about local health conditions, about practices and customs, is also essential. It is not just about finding a molecule in the laboratory, and a new cheap medicine out of it. It is also and crucially about understanding the context in which that medicine actually works, and can be administered in the most effective way. Local medical expertise on the ground is vital. Last but not least, PDP's have resources in the form of legitimacy. At face value PDPs enjoy legitimacy from their good-will and wish to solve problems for the global poor. Yet

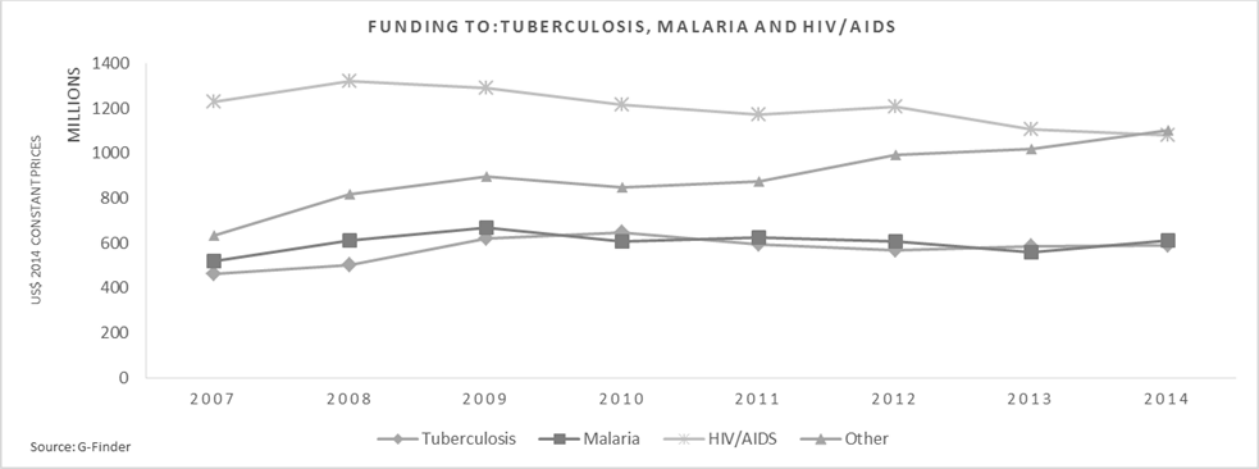
legitimacy is not a resource that must be taken for granted. It comes from different sources, such as the endorsement of key stakeholders to the overall goal (patient organizations, local authorities, or national governments); as well as by the consistency, coherence and ethical nature of the PDP's own management of the processes.

Those resources must be put into work for providing successfully the seven different functions along the complex value chain of new medicines. The extent to which PDPs have managed to do so is an empirical question. Section 4 below will characterize different types of PDPs, which will allow examining in more detail how are resources put at play to fulfil these self-defined functions. They empirical analysis will be conducted in the subsequent sections, identifying the patterns by which individual PDP's have put the four resources into play for providing the expected outcomes. The diversity of PDP's will allow to identify similarities and differences across the different types, helping to understand how the nature of PDP's somehow shapes the way in which those resources are allocated, distributed and mobilized in such complex contexts and with such ambitious goals.

4. Characterizing Product Development Partnerships for Neglected Diseases: Origins and Types

There are today around two dozen different product development partnerships. Most of them were created around the year 2000 in relation with increasing concerns about diseases associated to important health problems in developing countries. Somehow they are associated to the UN initiative of the Millenium Development Goals put forward in the turn of the millennium, others are associated to long-standing efforts in specific diseases. The three most important diseases that represent the bulk of PDP activities are Malaria, AIDS-HIV and Tuberculosis. Other 18 neglected tropical diseases like Leishmaniasis, Chagas or Dengue, have been identified by WHO on the basis of their relevance for health in some tropical areas, and that affect around one billion people. The table below shows the share of funding that goes to the 3-large diseases in comparison to these other tropical diseases. Some authors argue that these three main large diseases have received the most attention during the period 2000 2015, and that only after the launch of the sustainability development goals by the UN, the other diseases received increased attention.

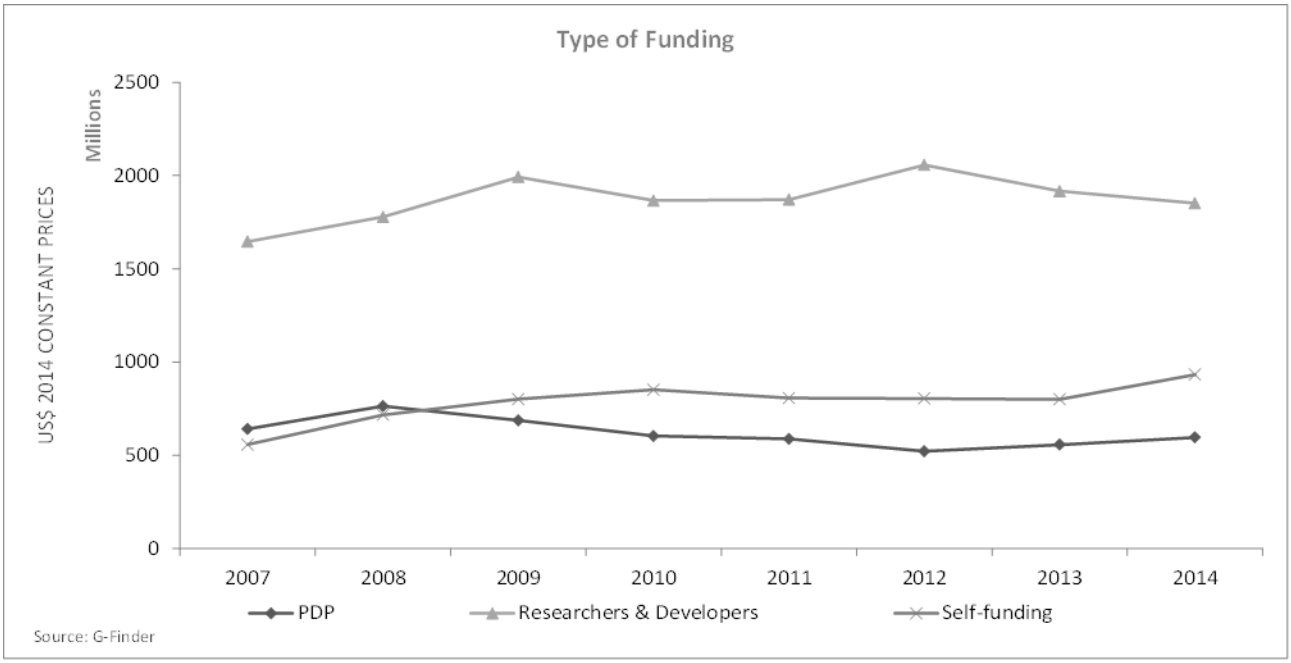
Figure 1: Amount spent on three selected neglected diseases compared to the other neglected diseases (2007-14). Million USD in 2014 constant prices



Source: G-Finder database

It is worth noting that there are several ways of funding research and innovation in neglected diseases. Sometimes national governments, international organizations, private philanthropies and other donors, fund research and innovation in those diseases by giving them directly to specific projects; other times they conduct research and innovation activities themselves; and third but not last, they might fund product development partnerships. The figure below shows the relative share of these three ways of funding. The figure shows that PDP's are a considerable funding mechanism these days. For that reason some experts argue that there are two regimes of global health today, one that is based on market and private production of medicines through the legal protection of intellectual property rights; and another regime that is based on product development partnerships which is quite different from the other one (Williams 2012). There might be a point in that, however the size of investment in these neglected diseases continues to be substantially lower than the size of investment in other diseases that afflict developed countries. In other words, these two regimes are not only structurally different, but also content-wise different. To a very large extent, the rise of PDP's is highly associated to the rise of new forms of philanthropy and their active role in promoting global health (Rushton and Williams 2011) (Eckl 2014).

Figure 2: Types of Funding All Neglected diseases (2007-2014). Million USD in 2014 constant prices.



Source: G-Finder Dataset

PDP's share generally at series of features, like their focus on providing accessible medicines for diseases afflicting patients in developing countries, as well as some of the basic organizational features in the form of partnership. However, in spite of sharing similar goals and overall expectations, these partnerships differ significantly in their structures, funding sources, knowledge expertise, strategies, and interaction with public health authorities. This is so because they have very different origins, and most important for this paper, they fulfill different functions and enjoy very different resources. For that reason, it might be worth to examine the different types of PDPs in order to understand this variety.

Table 1: Disease and type of medicine by PDP

Name of PDP	Disease	Treatment	Vaccine	Other (diagnosis, insecticides)
International AIDS Vaccine Initiative (IAVI) https://www.iavi.org/	HIV/AIDS		X	
Malaria Vaccine Initiative (MVI) www.malariavaccine.org (also known as PATH-MVI)	Malaria		X	
Drugs for Neglected Diseases initiative (DNDi) https://www.dndi.org/	Visceral Leishmaniasis (VL), Human African Trypanosomiasis (HAT), Chagas, Pediatric HIV, Filiarial diseases, Mycetoma, Hepatitis C	X		

	and Malaria			
European Vaccine Initiative (EVI) http://www.euvaccine.eu/	Dengue, Influenza, Staphylococcus aureus, Para-typhoid project.			
Innovative Vector Control Consortium (IVCC) http://www.ivcc.com	Vector-borne diseases like Malaria, Dengue, etc.			
AERAS Global TB Vaccine Foundation http://www.aeras.org/	Tuberculosis			
OneWorld Health (OWH) Became part of PATH in 2011 http://oneworldhealth.com/				
International Vaccine Institute (IVI) http://www.ivi.int/				
Medicines for Malaria Venture (MMV) https://www.mmv.org/	Malaria			
Meningitis Vaccine Project (MVP) www.meningvax.org Part of PATH	Meningitis A			
Pediatric Dengue Vaccine Initiative (PDVI) **www.denguevaccine.org**				
Sabin PDP www.sabin.org			X	
South African AIDS Vaccine Initiative (SAAVI) www.saavi.org.za			X	
TuBerculosis Vaccine Initiative (TBVI) www.tbvi.eu	Tuberculosis		X	
Dengue Vaccine Initiative (DVI) www.denguevaccines.org				
The Consortium for Parasitic Drug Development (CPDD) **www.thecpdd.org**				
TB Alliance **https://www.tballiance.org**	Tuberculosis			
Infectious Disease Research Institute **(**IDRI) **www.idri.org**				
Reproductive Health and HIV prevention (CONRAD) **www.conrad.org**	HIV			X
HIV Vaccines Trials Network (HVTN) **www.hvtn.org**	HIV		X	
International Partnership For Microbicides **(**IPM) **https://www.ipmglobal.org**	HIV			X
Microbicides Development Program (MDP) **www.mdp.mrc.ac.uk**	HIV			X
FIND **www.finddx.org**	Tuberculosis, malaria, HIV/AIDS, sleeping sickness, hepatitis C,			X

	leishmaniasis, Chagas disease, Buruli ulcer, febrile illnesses and other infectious diseases			

Source: Further own elaboration from Table 2 in (Muñoz, Visentin et al. 2014).

Generally speaking, the product development partnerships can be classified according to two dimensions. The first dimension goes from PDP's that tackle single diseases to PDP's that tackle multiple diseases. The second dimension is a continuum that goes from one type of medicines to several types of medicines (like vaccines, treatment, diagnosis etc.). This gives a matrix of 2×2 types of PDPs. The wider the PDP's targets are, the more complex the tasks that they will have to address. For example, the PDP on tuberculosis alliance which focuses only on one disease and in one on one type of medicine (vaccines), has a more straightforward tasks than the PDP which focuses on several diseases and on several types of medicines at once, like for example Drugs for Neglected Diseases initiative (DNDi). The wider the portfolio of projects, the more resources are required to implement them successfully.

The current paper has selected for most emblematic case studies of PDP's. They were all created at around the same time, at the beginning of the millennium, and share similar goals in terms of fostering transformative change in the prevention, cure and reduction of these neglected diseases for the global poor. However they differ in terms of the range of tasks they have set up for themselves, which defines the number of projects and areas of activity. We can therefore see that analyzing the three cases in comparative perspective will bring forward a better understanding of the functions they fulfil, and there relative association to the subsequent resources they have at hand. The three cases we have selected are: DNDi, EVI, and PATH-MVI. Next section explores them.

5. The Cases Under Study

The selection of the cases under study has been made on the basis of the 2×2 metrics mentioned in the previous section. This will allow to see differences across the PDP's. The more ambitious they are in terms of number of diseases and number of functions they aim at fulfilling (the wider their span of action is), the more complex and resource-dependent they will be. In other words, the wider they are, the more resources they need to mobilize in order to fulfil them.

Table 2: The Selection of Four Cases

	Multiple Diseases	Single Disease
All stages in the product development value chain	DNDi	
Early or Late stages in the product development value chain	EVI	MVI-PATH

Source: Own elaboration

Table 3: The functions of the 4 cases

Functions	DNDi	EVI	MVI-PATH http://www.malariavaccine.org/about-us
Advocacy & communication	X	Very limited	X
Support R&D conducted by others	X	X	
Conduct in-house research	X	X	
Conduct development & clinical trials	X	Early clinical trial phases	X
Integrate R&D knowledge from others	X	X	X
Negotiate and guide the process securing access and affordability of drugs	X		X
Assist implementation of drug introduction into the health systems.	X		X
Assist harmonizing regulatory frameworks		X	
Build up capacity in R&D in less developed countries		X	

Source: Own elaboration

The Malaria Vaccine Initiative (MVI), (in other places called PATH-MVI) is a partnership focusing on providing a vaccine for Malaria. It was created in 2001 with a large donation by Bill and Melinda Gates Foundation. It is generally acknowledged to have the most advanced form for vaccine for Malaria until

date. The name of the vaccine is RTS,S, and is being currently developed by MVI and GlaxoSmithKline (GSK) in partnership. It has a protective efficacy of less than 50%, but still is the most effective to date among other vaccines against Malaria. Moreover, beyond its own benefits, "the work on RTS,S has given valuable lessons, and helped develop regulatory pathways for malaria vaccines". (Boulton, Meredith et al. 2015) (p.29). According to their webpage: "MVI maintains a diverse portfolio of preclinical, early clinical, and advanced clinical projects", so RTS, S is not the only project ahead. Generally, MVI picks up the opportunities offered by some previously discontinued research projects, typically by private firms, who did not see sufficient economic or medical incentive to work further on those projects. This is not only the case of MVI, other PDPs also tend to re-use these discontinued projects (Pedrique 2013). That was also for RTS, S, because it was a project that was discontinued in 1987. The current agreement for this RTS,S is: "The pricing arrangement announced for the RTS,S vaccine for young infants and children in Sub-Saharan Africa is that GSK will be paid to cover the costs of the vaccine manufacturing and will receive a 5% return." (Muñoz, Visentin et al. 2014) p. 13.

DNDi was founded by 6 partners in the early 2000s, among which the NGO "Medicines sans frontiers" is a very prominent founding member as well as donor. DNDi has a specially close relationship with WHO, which sits as an observer in the board. DNDi's organization is rather strong, with a very well experienced board members, as well as a strong scientific advisory committee, both overseeing the strategy and decisions of executive management. Since 2007, DNDi has delivered 1 new treatment per year and has met its 2007 target of 6 novel treatments by 2014. Following some authors, "These are all low-hanging fruits that could be developed rapidly and with a high probability of success as they are either re-purposing existing drugs or developing combinations" (Boulton, Meredith et al. 2015) (p. 8). DNDi has aimed at diversifying its sources of income as much as possible, which has managed to do. Yet, as in other PDPs, during the past years more and more donors provide their funding in a restricted manner, meaning, in a way that the donor decides more or less in detail which projects to fund. This contrasts with the unrestricted funds, which are available for the PDP to decide entirely upon. "DNDi does accept funding restricted to individual projects, but the ultimate decision-making on the progression of individual projects remains with DNDi". (Boulton, Meredith et al. 2015) (p.9). When looking at the latest available data, it seems that restricted funding accounts for around 65% of all DNDi funds. DNDi is generally considered one of the most solid and successful PDPs to date. Yet the effectiveness of some of its medicines has been discussed in recent times (Chatelain and Ioset 2011).

The European Vaccine Initiative (EVI) is registered in Germany as a not-for-profit European Economic Interest Grouping (EEIG). It was founded by the Universities of Stockholm and Heidelberg, and today has four other funding members. "This EEIG construct gives ownership of the organisation to its members (representing the member states) and aims to create a more active involvement of both the founders and their countries. However, in practice it appears to be a fairly cumbersome structure and some stakeholders as well as the American Appraisal's evaluation questioned whether the EEIG is the most appropriate construct for EVI." (Boulton, Meredith et al. 2015 (p.28). Compared to the other two PDPs studied here, EVI has a very reduced organizational size. "EVI is a small organization - only 16 staff with 11 FTE, compared with 48 full time staff at FIND and over 100 at DNDi (the Path MVI currently has a staff

of around 40 FTEs although it has had over 60 before)". EVI works differently than the other two cases of PDPs in this paper. It supports specific R&D projects that are funded through public calls from the EU or national levels. Those projects are brought together and receive additional funding. Some projects are proposed to the board, which takes the decision to support them if they fulfill some specific criteria. Therefore EVI promotes projects that are already in place, supporting them additionally in order to reach the goal of affordable and accessible medicines. In fact EVI expanded its scope from Malaria vaccine to other vaccines of neglected diseases.

EVI specializes in the early phases of the value chain of medicine production, which are research, preclinical and early clinical stages. It collaborates closely with The European & Developing Countries Clinical Trials Partnership (EDCTP), which is in charge of late stages of clinical trials. For that reason, EVI can be seen as a bridge and coordinator between different early phase R&D projects, and as a bridge towards later phases of the value chain. "To date it has funded 24 malaria antigen combinations in 32 vaccine formulations and taken 1632 candidates to phase I clinical trials." (Boulton, Meredith et al. 2015) P 29.

6. Conclusions

There continues to be today a debate about the extent to which the PDPs focus on neglected diseases is effective or not; yet some individual success stories are starting to emerge (Molyneux and Malecela 2011) (Bishai, Champion et al. 2011). Most of the challenges of the PDPs have to do with the technical difficulties to crack down these complex diseases (Bethony, Cole et al. 2011) (Matlin, de Francisco et al. 2008); whereas others have to do with the problems associated to organizational issues (Moran, Guzman et al. 2010). However, they are gradually constituting essential ways of dealing with these difficult issues, addressing grand societal challenges associated to health among the poorest in the world (Chataway, Hanlin et al. 2009, Chataway, Hanlin et al. 2010). Highly associated to the Millennium goals of the UN, these PDPs are still very different in their organizational structure and ways of operation. However, they share the ultimate ambition to provide cheap and accessible medicines to these patients. Their rapid creation has recently induced towards more coordination and synergy across them. And in this regard some specific coordination initiatives have developed recently (Grace 2010).

The three cases examined are among the most successful PDPs to date. All three have very strong organizations and secretariats, as well as specific founding members that are very active and engaged: MVI (PATH and GSK), DNDi (Medicines sense Frontiers), and EVI (the European Commission). These are very strong and capable agents who have been able to provide the PDPs with four essential resources: funding, organizational, knowledge and legitimacy. Regarding the first, two of the cases examined have been largely funded by philanthropies, in particular the Bill and Melinda Gates foundation; whereas EVI is largely founded with public means of R&D activities. As we have seen above, these resources have been essential for the initiation and continuation of the PDPs. Most interesting, DNDi has had a strong focus on avoiding the dependence on too few sources of funding; initiating great efforts to diversify

their sources of income. Regarding organizational resources, all three PDPs have created separated organizations which manage the economic resources and the portfolio of projects. However, these organizations vary greatly: whereas MVI and DNDi have medium-size organizations, the EVI has a very small secretariat. This seems to have limited EVI's ability to extend its portfolio of activities. The quality of project management is rather high, as the secretariats have experience and organizational managerial abilities. The third resource is knowledge. The three PDPs have enjoyed from high levels of medical professional expertise and knowledge. Some well-known medical professionals have actively engaged in the PDPs, providing important forms of knowledge resource, which is necessary for making critical decisions about project portfolio in context of limited resources. Last but not least, legitimacy has been an essential resource in these PDPs. Aware of the importance of legitimacy for the operability of these partnerships, they have been very careful to fulfill high international standards of safety in their clinical trials, as well as tying to be as transparent regarding their operations. Legitimacy is not just about limiting the risks and securing safety. It has to do as well with the perception of the general public about the importance and viability of the PDPs. For that reason, these organizations have made significant efforts to remain visible in the public sphere, and to conduct awareness raising about the problems that these neglected diseases continue to pose to global health.

The strength and capability of the major actors engaged in these PDPs has allowed them to make the most of the opportunity structures emerging, either in terms of attracting further resources, but most importantly, in terms of providing the first positive results in some drug development that was previously abandoned. Whereas there is considerable way ahead for solving these grand social challenges, the first steps are promising, and PDPs seem to be valuable transnational governance arrangements in the field of global health.

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