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Abstract

This study concerns the economics of innovation in the area of medical innovation –new diagnostics, medicines and vaccines-, and in particular how innovation contributes to meeting public health needs. Significant advances have taken place in medical science and technological innovations to prevent and treat diseases that are associated to the strong research and innovation system characteristic of the biomedical and pharmaceutical industry in developed countries. However, firms are reluctant to mobilize this capacity towards disease areas where there are significant health needs but the market is not profitable. As a result, less socially valuable innovation takes place than would otherwise be desirable. This problem is treated in this study through institutional analysis, applied to the area of neglected diseases. The term neglected diseases is used to refer to a group of diseases that affect over 1 billion people worldwide, persist under conditions of poverty and are concentrated mainly in developing countries.

Previous studies of the problem of the gap of innovation in neglected diseases have focused on identifying the market failures that cause for-profit firms to invest very little in research and development (R&D) and innovation in neglected diseases, and advance ideas for new or additional incentives that could encourage greater participation of firms in this area, such as guaranteed payments for R&D efforts or new medical products developed. This study takes on a different approach, centred on analysing the institutional framework in which R&D and innovation dynamics take place. In particular, the study analyses a recent phenomenon: the appearance of a new form of institutional experiment – private non-profit entities organized as product development partnerships (PDPs) that act as "system integrators" to leverage the resources and capabilities of a network of public, philanthropic and private sector partners towards R&D in neglected diseases.

The study also examines how this novel PDP institution responds to a well-known incentive mechanism in medical innovation – intellectual property rights. The study finds that PDPs respond differently to IPRs than for-profit firms, and this indicates there are variations in the value, use and impact of IPRs under different institutional settings, beyond the firm.

Finally, the study analyses the challenges in leveraging traditional medicinal knowledge to address health needs, particularly in developing countries, and finds that as the traditional institutions that have supported traditional medicine are under strain, new institutions are needed to support this knowledge as it becomes fragile and is more likely to suffer from deterioration or even disappearance, as compared to scientific knowledge.

Keywords

Innovation, medical products, institutions, public health, neglected diseases, product development partnerships, Intellectual property rights, traditional medicine

Résumé

La présente étude porte sur l'économie de l'innovation dans le domaine de l'innovation médicale (nouvelles méthodes diagnostiques, nouveaux médicaments et nouveaux vaccins) et explique, plus particulièrement, comment l'innovation contribue à répondre aux besoins de santé publique. La science médicale et l'innovation technologique ont fait d'immenses progrès dans la prévention et le traitement des maladies notamment grâce au système solide de recherche et d'innovation qui caractérise l'industrie biomédicale et pharmaceutique des pays développés. Pourtant, les entreprises sont peu disposées à utiliser cette capacité dans des domaines pathologiques où les besoins sanitaires sont importants, mais représentent un marché peu rentable; si bien que l'innovation socialement utile est moins profuse que ce qu'il faudrait. Dans la présente étude, le problème est analysé sous un angle institutionnel, appliqué au domaine des maladies négligées. L'expression « maladies négligées » se rapporte à un groupe de maladies qui touchent plus de 1 milliard de personnes dans le monde, se manifestent plus fortement là où sévit la pauvreté et se concentrent principalement dans les pays en développement.

Les études qui se sont déjà penchées sur le problème du manque d'innovation en matière de maladies négligées avaient principalement pour but d'identifier les défaillances du marché qui expliquaient les faibles investissements des entreprises à but lucratif dans la recherche-développement (R-D) et l'innovation des maladies négligées, et proposaient des mesures incitatives nouvelles et additionnelles susceptibles d'encourager les entreprises à s'impliquer davantage dans ce domaine, comme les paiements garantis pour récompenser les efforts en matière de R-D et la mise au point de nouveaux produits médicaux. La présente étude est, quant à elle, axée sur l'analyse du cadre institutionnel dans lequel les dynamiques de la R-D et de l'innovation ont lieu. Plus précisément, l'analyse concerne un phénomène récent : l'émergence d'une nouvelle forme d'expérience institutionnelle où des entités privées à but non lucratif s'organisent en partenariats pour l'élaboration de produits qui agissent comme des « intégrateurs de systèmes » afin de rassembler les ressources et les capacités d'un réseau de partenaires publics, philanthropiques et privés dans la R-D relative aux maladies négligées.

L’étude examine également comment ce nouveau dispositif institutionnel de partenariat pour l'élaboration de produits s’accorde avec un mécanisme d'incitation connu dans le domaine de l'innovation médicale, nommément les droits de propriété intellectuelle. L’étude fait apparaître que les partenariats ne s’adaptent pas de la même manière aux droits de propriété intellectuelle que les entreprises à but lucratif, ce qui montre que l’utilité, l’usage et les effets des droits de propriété intellectuelle varient en fonction des contextes institutionnels, qui sont extérieurs à l'entreprise.

Pour finir, l’étude analyse les problèmes qui se posent pour mobiliser les connaissances médicales traditionnelles afin de répondre aux besoins sanitaires, notamment dans les pays en développement, et conclut qu’étant donné que les institutions traditionnelles qui ont encouragé la médecine traditionnelle sont en difficulté, de nouvelles institutions sont nécessaires pour assurer la subsistance de ces connaissances qui se fragilisent et risquent de se détériorer, voire de disparaître, par rapport aux connaissances scientifiques.

Mots-clés

Innovation, produits médicaux, institutions, santé publique, maladies négligées, entités privées à but non lucratif, propriété intellectuelle, médecine traditionnelle

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Chapter 1 Introduction

This study examines the role of medical product innovation and supportive institutional environment –the rules of the game- to meet health needs. In particular, it examines the challenges of spurring medical innovation to tackle diseases that pose a disproportionately high burden to poor populations in developing and least developed countries, and focuses on the institutional framework that can be developed to effectively respond to the challenges. It also examines the difficulties in leveraging the potential of traditional medicinal knowledge to address health needs, particularly in developing and least developed countries.

Why are global research and development (R&D) priorities as defined by market-oriented for-profit firms to a large extent disconnected from public health needs? Is institutional change or experimentation taking place to effectively respond to this problem? Can the institutions that work well to support the biomedical and pharmaceutical industry be extended to the area of neglected diseases? These are some of the questions that are addressed in this study.

Overall, the study finds that there is need for recognition that there can be multiple of ways of organizing innovation and institutional arrangements and incentive mechanisms to support innovation. These need to be well matched to the specific socio-economic context to solve pressing social dilemmas. The study contributes to the understanding of R&D in a non-profit context and the importance of collaboration and non-market institutions to promote innovation where market failures occur. The study also highlights that the value, use and impact of specific institutions associated to R&D and innovation can vary under different settings, informed by the example of how intellectual property rights (IPRs) are managed by PDPs. Finally, the study contributes to the understanding of the value of traditional medical knowledge for public health and the role of traditional institutions that support this form of experimental knowledge.

1.1 Theoretical Approach

Health is essential to human well - being[1]. Not all people have the same capabilities – opportunities- to achieve good health (Sen, 2002). While many social, economic, environmental factors and personal choices that influence health, some populations are more vulnerable to poor health. These include those in the lowest socioeconomic position, across and within countries (CSDH 2008). Reducing health inequity, such as inequalities in health care – including inequalities in availability or access to interventions to address health needs- that are socially constructed, unfair and therefore correctable-, is an aspiration generally shared across health disciplines and practitioners. It is also supported by human rights law for the realization of the right to health that every human being is entitled to the enjoyment of the highest attainable standard of physical and mental health.[2] These perspectives in turn strongly inform public health and global health policy, a domain in which governments play a central role.[3]

Economics, particularly welfare economics and health economics, is likewise influential in understanding the production and distribution of health care and informing public health policy. With respect to the treatment of concerns of health equity, overall these are less present in economic policy analysis as compared to public health and human rights (economics is generally more concerned with maximizing growth or aggregate social utility). The functioning of society is analyzed mainly through the lens of market organization, as opposed to other alternative social arrangements. Orthodox economic theory holds that rational, self-interested individuals participating in

[1] The World Health Organization definition of health is "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948.

[2] The right to health is recognized in the 1948 Universal Declaration of Human Rights (UDHR) and the 1966 International Covenant on Economic, Social and Cultural Rights, Article 12. It is discussed in detail in the General Comment No. 14 of the United Nations Committee on Economic, Social and Cultural Rights, E/C.12/2000/4. Government obligations in relation to the right to health include providing access to affordable and quality health care for all.

[3] The concept of "global health" is often used interchangeably with public health (at a global scale), international health, or global public health. Some common elements emphasized are health as a public good -benefit all members of every society-; priority on a population-based and preventive focus; concentration on poorer, vulnerable, and underserved populations; multidisciplinary; importance of systems and structures; and the participation of several stakeholders (Koplan et al 2009). Global health also denotes a notion of health interdependence and risk across national borders due to cross border flow of people and products. (Frenk and Moon 2013).

open markets –competition and well-functioning pricing system-, should provide the optimal outcome that enhances overall economic growth and welfare for society. Thus, economic policy has largely focused on analyzing how a given situation can be brought closer to this ideal.

A broad criticism of this approach is the largely abstract nature of the analysis, devoid from real world experience; what R. Coase termed "blackboard economics". Coase (1937) prominently showed that there are costs to using the price mechanism for coordinating economic activity that explained why alternative institutional arrangements, -primarily the firm-, surface to coordinate economic activity at a lower cost. Coase also argued that when property rights are well defined and transactions costs are low, private parties can organize among themselves to internalize (solve) externalities– the costs or benefits of market transactions that affect an uninvolved third party to the transaction (Coase 1960). Likewise, K. Arrow in a seminal work focused on the health care industry showed that the functioning of the industry and its ability to satisfy the needs of society differs from the precepts of orthodox economics, and advanced that when the market fails, social institutions are created to attempt to address the gaps (Arrow 1963). Institutions can be broadly understood as "the rules of the game" that structure interactions, reward and regulate a variety of actors interacting in the economy.

The existence of various forms of markets failures and the importance of institutions to address these is now well accepted and is widely applied as a framework of economic analysis. Market failures find explanation in various factors, including transaction costs, externalities, information asymmetries, mismatched incentives, and lack of supportive institutions. However, the approach of understanding the dynamics in the economy through the lens of market failures is not without critique, particularly from evolutionary and new institutional economics (Nelson and Winter 1982, Williamson 2000) that aim to broaden the analysis to include market and non-market institutions that influence economic behavior. As noted by Nelson (1990), "active policy analyzed as response to "market failures" is not adequate as it gives privilege standing to market organization, and supplements to market organization or different forms of organization or financing of an activity are placed in a position of 'second best' solution justified only because markets 'fail' in some sense. Better to see that different kinds of financing, and different kinds of organization, are better for different kinds of things, instead of viewing the markets as preferred general purpose model of operation, except when they fail. Analysis of different forms of different ways of organizing, governing and funding an activity should proceed without bias."

This study also follows the approach that economic analysis of a socio-economic problem requires understanding to the specific context for the functioning of the market and non-market elements of the economy and in particular, the underlying institutions. Furthermore, the study also considers that market failures remain a valid and useful approach, though not sufficient, to think about how alternative institutional arrangements and policy interventions can correct for less than socially optimal outcomes because of the extent of use or influence of markets in most economies and societies. Combining the market failure approach with institutional analysis provides a broader and more realistic framework of analysis to consider potential alternative arrangements to markets to direct medical innovation towards meeting public health needs.

1.2 Chapters

The study is organized in three chapters. Chapter 1: "Can medical products be developed on a nonprofit basis? Exploring product development partnerships in neglected diseases", begins by providing a context of the problem of lack of R&D and medical innovations to diagnose, prevent and treat diseases that have a large burden in developing countries but no or small burden in the developed world. In the past decades, significant advances have taken place in medical science and technological innovations health, including developing new diagnostic tools, vaccines and medicines to prevent and treat diseases. These are related to the strong research and innovation system characteristic of the biomedical and pharmaceutical industry in developed countries (Cockburn and Stern 2010). The system, however, has not been unable to address a number of problems. The specific problem addressed in this chapter is the lack of new medical products in the area of neglected diseases. The chapter analyses a recent phenomenon: the appearance of a new form of institutional experiment –product development partnerships (PDPs). We define for purposes of our study PDPs as self-governing, private, non-profit organizations that aim to develop new medical products in the area of neglected diseases. The chapter examines closely PDP institutions, in particular how they address knowledge externalities and solve coordination problems in the complex area of R&D for medical innovation for neglected diseases. A key finding is that PDPs act as "system integrators" to leverage the resources and capabilities of a network of public, philanthropic and private sector partners towards R&D in neglected diseases.

Chapter 2 explores in detail the institution of intellectual property rights (IPRs). While it is considered to provide important incentives for R&D and innovation in the biomedical and pharmaceutical industry, so far there is no evidence as to whether IPRs play a similar role in context of PDPs in the area of neglected diseases. The study finds that IPRs does not act as an incentive for the R&D activities of PDPs, but PDPs do use IPRs for strategic purposes to advance their non-profit and access mandate. A broad conclusion of this chapter is that the research on economics of IPRs should be informed by institutional analysis to deepen understanding of the variations in the value, use and impact of IPRs under different institutional settings, beyond the firm.

Finally, Chapter 3 explores the value and role of traditional medical knowledge in addressing public health needs. The weakening of traditional institutions to support the production and diffusion of traditional medical knowledge is associated to loss of knowledge, which to reduced capacity for effective action in certain socioeconomic contexts and circumstances in which such knowledge was previously useful or can be useful. As this system of institutions becomes less robust and is collapsing, then the question of what socio-economic institutions can be relied upon to produce and distribute experiential knowledge in an efficient manner becomes central. The chapter examines to what extent the institutions that support scientific knowledge could be extended to the case of experiential knowledge, as a substitute of the traditional institutional framework that is slowly disappearing.

Chapter 2 Can medical products be developed on a not-for-profit basis? Exploring product development partnerships for neglected diseases[4]

Reliance on market forces can lead to underinvestment in social welfare enhancing innovation. The lack of new medical products in the area of neglected diseases is a case in point. R&D for neglected diseases has increased with new funding and collaborations taking place mainly through product development partnerships (PDPs). PDPs are self-governing, private non-profit R&D organizations. In contrast to push and pull instruments designed to address private-sector R&D underinvestment, PDPs have emerged voluntarily to address this public health challenge. In this study we examine how non-profit R&D collaboration for neglected diseases takes place through PDPs. We find that PDPs act as 'system integrators' that leverage the resources and capabilities of a network of public, philanthropic and private-sector partners. This study contributes to an understanding of R&D in a non-profit context and highlights the importance of collaboration and nonmarket institutions for promoting innovation where market failures occur.

2.1 Introduction

Over a billion people are affected by diseases that have a large burden in developing countries, but no or small burden in the developed world (World Health Organization 2010). Historically, government public health programs and the pharmaceutical industry have neglected these poverty-related diseases. Very few new medical products (drugs, vaccines and other biological pro-

[4] This Chapter is published as Muñoz-Tellez, V., Visentin, F., Foray, D., Gaule, P. (2014) 'Can medical products be developed on a not-for-profit basis? The case of Product Development Partnerships', Science and Public Policy, doi: 10.1093/scipol/scu049.

ducts, diagnostics and vector control products) are developed for their prevention and treatment. Pharmaceutical firms, absent market incentives to spur their commercial interests, are reluctant to independently engage in these endeavours. As a result, they pass up opportunities for socially valuable innovation.

Economists have proposed a range of economic instruments to incentivize firm-level R&D in neglected diseases. Push mechanisms that aim to bring down firms' costs of R&D, such as grants, tax credits and loans are more broadly used by policy-makers. Pull mechanisms, on the other hand, such as milestone or end prizes, aim to increase market attractiveness by lowering the risk of R&D and assuring revenue for the outputs.

Meanwhile, a rising number of self-governing private non-profit organizations have emerged to catalyse R&D for neglected diseases. Product Development Partnerships (PDPs) have produced various new diagnostics and therapies in the form of reformulated or repurposed versions of existing drugs, vaccines and biological products. They have also built significant R&D project portfolios with several novel vaccines and drug candidates in the pipeline, including new chemical entities (NCEs). Most PDPs do not undertake any in-house R&D activities, but rather operate through external collaboration. PDPs mobilize funding from philanthropic and public entities and partner with a number of public and private institutions to implement R&D projects, including academia and public research institutes, pharmaceutical, biotechnology and other private for-profit firms, such as contract research organizations.

This PDP openness to external R&D collaboration can appear to mirror a similar trend in the pharmaceutical and biotechnology industry (Juliano 2013). However, the motivation for PDPs to pursue R&D collaboration is distinctly associated with their non-profit mission. Large pharmaceutical firms are increasingly sourcing their R&D portfolios by in-licensing external R&D projects and through mergers and acquisitions (M&A) to raise growth and revenue prospects (Schuhmacher et al 2013). In contrast, the common goal of PDPs is to build R&D portfolios to develop products that address unmet health needs. This means that the final product must be affordable and accessible to patients. In this context, partners involved in PDP-led R&D projects have to operate within the confines of the PDP mission. The concept of "partnership" implies a commitment to a common goal through the joint provision of complementary resources and expertise, and the joint sharing of the risks involved (Ridley 2001).

This research is informed by a literature review and in- depth interviews with the staff of PDPs. Previous literature has described the role of PDPs in the neglected disease landscape (Moran 2005, Grace 2006, Chataway et al 2007, Grace 2010, Moran et al 2010, Chataway et al 2010). While building on this literature, we further explain the operation of PDPs, identify their core capabilities, provide an update of PDP outputs, and analyse the variety among PDPs and the constraints of the PDP approach.

The study is divided into seven sections. Following the introduction, the second section presents the problem of insufficient innovation for neglected diseases. The third section then describes the economic instruments that are designed to stimulate innovation in neglected diseases. The fourth section explores how PDPs access and leverage external resources and capabilities through R&D collaborations. The fifth section explains the variety within the PDP landscape. The sixth section discusses the limitations of the PDP organizational form. The seventh section concludes.

2.2 The shortfall of innovation for neglected diseases

The "neglected disease" expression points out the problem of insufficient new medical products developed to address diseases that create a large burden in developing countries, but little or no impact in the developed world. There is no single definition of "neglected disease". The WHO defines "neglected diseases" as a group of 17 diseases affecting more than 1 billion people worldwide that persist under conditions of poverty and are concentrated almost exclusively in impoverished populations in developing countries (World Health Organization 2010).[5] Infectious diseases in particular account for 10 million deaths each year, of which more than 90 percent occur in developing countries (World Health Organization 2010). For the purposes of our study, we consider the WHO- listed diseases and also include three communicable diseases: tuberculosis, malaria and HIV/AIDS.[6] These are diseases prevalent in developing countries that often they co-exist with other neglected diseases. However, they differ from other "neglected" diseases in that they may

[5] The diseases concerned are: Buruli ulcer; Chagas disease; cysticercosis; dengue; dracunculiasis; echinococcosis; endemic treponematoses; foodborne trematode infections; human African trypanosomiasis; leishmaniasis; leprosy; lymphatic filariasis;, onchocerciasis; rabies; schistosomiasis; soil-transmitted helminthiases; and trachoma.
[6] The inclusion of these diseases is consistent with other studies, i.e. Trouiller et al. 2002 and the G-FINDER Report on Neglected Disease R&D, 2012.

also be found in developed countries (e.g. tuberculosis and HIV/AIDS) and generally receive more financing for R&D and delivery.

New medical products are essential to the prevention, control and elimination of disease. The current level of R&D for new medical products targeting neglected diseases is negligible relative to the health burden of these diseases. The imbalance is evident if we consider (i) the amount of R&D investment for neglected diseases compared to the global R&D investment for all diseases and the health burden of neglected diseases; and (ii) the number of new medical products developed for neglected diseases compared to other diseases.

One study has found that global R&D investments by the public, philanthropic and private sectors in neglected disease research in 2010 (approximately US$2.4 billion) accounted for only 1% of overall health R&D investments (US$240 billion) (Røttingen et al 2013). Funding for neglected diseases has slightly increased from an estimated US$ 2.8 billion in 2005 (Global Forum for Health Research 2008) to US$3.045 billion in 2011 (G-Finder 2012). The largest funders are public donors, with a total of US$ 1.9 billion in 2011, followed by philanthropic donors, with a total of US$525.1 million in 2011 (G-Finder 2012).

The small number of new medical products for neglected diseases, as compared to other diseases, is an indication of the persistent gap in innovation within this area. One landmark study found that between 1975 and 1999, 1,393 new drugs (excluding vaccines) were made available to the public; however, only 16 of these were meant for neglected diseases (Troullier et al. 2002). A recent study finds that of the 850 new therapeutic products (NCEs, new indications, new formulations, fixed-dose combinations, and vaccines and biologicals) registered in the period 2000 to 2011, only 37 (4%) were indicated for neglected diseases, comprising 25 products with a new indication or formulation, and eight vaccines or biological products. Of those 25 products, only 4 were NCEs. Only 1% of all registered clinical trials were for neglected diseases (Pedrique et al. 2013).

Generally firms invest in R&D with the expectation that the revenues generated from the sales of new medical products will increase as a result. They finance R&D from their own resources (profits), as well as from public support instruments, such as tax breaks and grants. Nonetheless, firms generally tend to invest less than the socially optimal levels of R&D. The reasons include high risks and costs, problems of R&D financing and incomplete appropriability of returns to R&D (Nelson 1959, Hall 2010). To address the appropriability problem, firms can seek legal protection for their inventions through government-granted patents that give the firms time-limited monopoly control

(e.g. manufacture, use, and sales) over the product. Patents support a firm's pricing strategy, aimed at setting a price as profitable as the buyer (there can be several possible buyers, such as government health authorities, insurers, prescribers/pharmacists, patients out-of-pocket) is willing to pay. Use of patent- protected inventions normally requires authorization of the patent holder. Only after the patent protection expires, generally a 20- year period, can any other firm produce and market a generic version of the product. This competition helps to bring down the product price.

The pharmaceutical industry has historically invested very little in R&D for new medical products within the area of neglected diseases. This is to be expected, as the market for neglected diseases does not offer firms many opportunities for profit, despite the gross unmet needs for treatment. Accordingly, the economic barriers to R&D in neglected diseases by private firms can be described as follows (Webber and Kremer 2001):

- Commercial markets are small.
- Individual purchasing power is limited, even though the number of patients may be very large.
- High R&D costs (estimated to be the same as for new medical products for other diseases) and the inherent risk in R&D will not be covered by returns on investments.

Moreover, patents as an incentive for the appropriability of R&D returns are not an effective mechanism to stimulate R&D in neglected diseases, given the absence of a profitable market, and rather may affect the availability of affordable medical products (World Health Organization 2006).

It can be assumed that the risks and costs of new product development for neglected disease R&D may be the same as for other diseases.[7] Medical product development is generally very costly, with a high risk of failure. However, precise data on R&D costs of pharmaceutical firms are generally unavailable or undisclosed. This is a critical constraint for the adequate design of economic instruments and their employment to incentivize R&D in neglected as well as in other diseases. When firms do provide cost data, it is not specified how the R&D costs are calculated, or what is

[7] There can be ample variance, depending on the disease (e.g. the extent of research and development gaps, market attractiveness) and type of product and means of undertaking clinical trials.

included in the cost (Morgan et al 2010). It is estimated that a drug in the form of a NCE may take between 13 –15 years, from discovery to when it is available on the market. For vaccines, the full R&D process may take 12 years. The levels of attrition (likelihood of project failure) can be close to 60%, higher in the discovery stage. Published estimates of the R&D costs diverge widely, with existing studies varying in methodologies, data sources, samples and time periods. For example, one recent study by health economists calculate that the net median R&D cost may be in the range of US$13 to 204 million, while existing estimates range from US$161 million to 1.8 billion (Light and Warburton 2011).

There are also no concrete data on the extent of R&D investment overall in medical products by pharmaceutical firms. While R&D costs have risen in the past two decades, revenues for pharmaceutical firms have increased six times faster, with net profits after taxes substantially higher than profits for all other Fortune 500 companies (Light and Lexchin 2012). At the same time, the overall rate of innovation in the pharmaceutical industry has been in decline. The number of total innovative new medical products approved has fallen since the 1990s, while many of those are “me too” drugs, rather than new chemical (or molecular) entities, and without significant therapeutic value.

2.3 Economic instruments to stimulate innovation in neglected diseases

In the last decades, various instruments have been designed, and some have been implemented to address the underinvestment problem illustrated above. With the aim of filling the gap between private and social returns to R&D in the field of neglected diseases, “push’’ and “pull’’’ instruments have been explored by public and philanthropic sectors for financing and increasing R&D efforts.

“Push” instruments aim to stimulate R&D by reducing the costs of R&D for the industry. These include instruments that pay for inputs to R&D, such as providing direct funding to research, particularly basic research, but may also extend to applied research (grants to universities, government public research laboratories, or for joint projects with industry), R&D tax breaks, direct grants for small firms, funding for clinical trials in developing countries, open innovation platforms, patent pools and related initiatives, fast track regulatory review (approvals), pre-competitive research platforms for sharing R&D costs and regulatory harmonization. Some of the problems associated with pull instruments are that they may not provide sufficient incentive for R&D by them-

selves. Incentives between grantees and funders may be imperfectly aligned, and the instruments are vulnerable to politization/lobbying (Sampath and Hedge 2011).

"Pull" instruments pay for the outputs of R&D. The main barrier considered is insufficient market attractiveness, rather than the high cost of R&D. Pull instruments aim to address the problem of a lack of commercial markets. They are designed to create demand for yet-to-be-developed products and effectively enlarge the market for medical products in neglected diseases. Pull instruments reward the output (new medical products developed) rather than pay for inputs to R&D. There is limited practical experience with pull instruments for neglected diseases.[8] One attractive feature of pull instruments is that they are less costly than other instruments, as they do not entail up-front payments. Money is spent only if milestones are reached or if new medical products are developed in accordance to pre-defined criteria. The specified criteria would be pre-set by the purchaser (e.g. government, philanthropic organization or international organization). The firm or other entity could then decide on the R&D strategy to deploy in order to meet the criteria. Once the milestone is reached or the product is developed, the disbursement of the committed money would be made, and the purchaser could make the product available to patients at low or no cost. Examples of pull instruments include prizes, funds for end-payments (such as the Health Impact Fund), funds that would allocate resources to any research organization,[9] and advance market commitments (AMC).

A critical condition of the pull instrument is that payment has to be attractive enough to provide incentives to the participant in the scheme. In theory, an adequate size of the incentive may vary

[8] An AMC program has yet to be tried for incentivizing new medical products. The first experience inof the design of a large-scale pull instrument was the AMC GAVI Alliance initiative, which has been in place since 2009 to make available existing pneumococcal vaccines. It was designed by a group of economists (Levine, Kremer et al. 2005). Governments and the Gates Foundation made a binding commitment of US$1.5 billion to fund the pilot AMC for which vaccine manufacturers could bid. In 2010, GlaxoSmithKline and Pfizer committed to supply 30 million doses of their pneumococcal vaccines for 10 years, which had recently been approved in Europe and the US (Synflorix and Prevenar-13) at a maximum price of US$3.50 a dose. The two vaccines were selling for an average of 40 Euros in Europe and US$90 per injection in the United States. Each manufacturer's share of the AMC funds is disbursed as a subsidy per dose, in addition to the tail price of US$3.50 US thus, the total price goes up to US$7 for approximately the first 20% of vaccine doses procured from each manufacturer (Cernuschi et al. 2011). The aim is to enable firms to quickly recover incremental investment costs incurred to allow the scaling up of supply capacity to serve GAVI-eligible countries faster through the WHO and UNICEF as procurement agents. The expectation is that the vaccines will be distributed to 40 developing countries that will pay 15 cents of the US$3.50, with the remaining cost covered by the AMC. The estimate cost per child receiving the vaccine is US$4,722 (Scudellari 2011). Some concerns that have been raised are the costs of the system, transparency by firms on vaccine manufacturing costs and profit margins, geographical scope, eligible purchasing agents, and entry of developing country producers that can lower the vaccine costs (MSF 2013).

[9] Some of these proposals include the Product Development Partnership Financing Facility (PDP-FF), the industry R&D Facilitation Fund (IRFF), the Fund for Research in Neglected Diseases (FRIND), and a fund within a global framework on health research and development. These proposals are reviewed in the 2012 report of the WHO CEWG, pp. 176-179. See WHO 2012b.

among participants. For private firms, it requires increasing the likelihood of returns to their R&D investments (at best, bring profits, at minimum, no loss). For other types of organizations, such as non-profit product development partnerships (PDPs), the size of the incentive required may be smaller. In the design of pull instruments, a crucial element is the amount of the commitments (including specifications, such as the doses to be purchased and purchase price) that would be required to provide a strong enough incentive to create a market that would surpass the barrier to R&D investment. Economist Michael Kremer foresaw that substantial industrial investment in neglected disease R&D would occur only if expected rates of return were broadly equivalent to those anticipated from R&D in conventional areas. However, without proper information on the actual costs of R&D, public resources may be wasted. Robust data on the costs of R&D for new medical product development should inform these decisions. However, as discussed earlier, existing estimates for medical product innovation are unreliable.

A different means to spur medical innovation is via open models, based on collaboration. In the discovery phase, open models of innovation rely on collaboration, sharing of information among volunteers and open access to data. Two examples of these projects that have been studied are CSIR Team India Consortium's Open Source Drug Discovery project (CSIR OSDD) and The Synaptic Leap's Schistosomiasis project (TSLS) (Ardan and Rottingen 2012).

Various pull and push mechanisms and alternative means for medical product innovation have been recently reviewed by an expert working group of the WHO (World Health Organization 2012).

2.4 Organizations to drive innovation in neglected diseases: Product Development Partnerships

Evidence suggests that collaboration in R&D for neglected diseases is increasing. One study has found that there are approximately 348 organizations from the private and public sectors (academic/research institutions, biotechnology companies and other medium and small firms, such as contract research organizations, and large pharmaceutical companies) participating alone or in partnership with each other in the development of a combined pipeline of 374 drugs and vaccines for 23 neglected diseases (BVGH 2012). The majority of collaborations are reported to be taking place through PDPs, with a 40% share of participation in the total number of projects (BVGH

2012). Another study has found that for the 123 new medical products in development in the period of 2000 to 2011, public organizations were involved in 66 products (54%), private industry in 28 products (23%), and private non-profit organizations (including PDPs, charities, foundations, and philanthropic institutions) in 19 products (15%), with the remaining 10 products (8%) involving a mix of sponsors. All three NCEs for neglected diseases were being sponsored by private non-profit organizations (Pedrique et al 2013). It also appears that large pharmaceutical firms are increasingly interested in joining PDP projects more than in undertaking their own. The annual report by IFPMA for 2012, lists 132 R&D projects for new medicines and vaccines (excluding HIV/AIDS) involving IFPMA member companies, of which 112 are projects with PDPs, and only 20 (15%) projects are firm-only undertakings.

PDPs in the past 15 years have become part of the puzzle of how to close the innovation gap for neglected diseases. One study found that the PDP pipeline included 63 neglected disease drug projects (excluding vaccines, diagnostics and microbicides) under way at the end of 2004, including two new drugs at the registration stage and 18 new products in clinical trials, half of which had already reached Phase III (Moran 2005). However, new projects have been launched since the end of 2004, amplifying this trend (BVGH 2012). A full list and description of new products developed by PDPs is found in Table 9 in the Appendix to this study.

Since the 1990s the number of PDPs has grown from one to 23 PDPs in 2014, which we have identified in our study.[10] We define for purposes of our study PDPs as self-governing[11], private, non-profit organizations that aim to develop new medical products in the area of neglected diseases. PDPs are not push or pull instruments for R&D. As discussed in Section 3, push and pull instruments are policy instruments designed mainly to promote private investment in R&D.[12] In con-

[10] Our complete list of PDPs includes, in alphabetical order: AERAS;, Contraceptive Research and Development (CONRAD); the, Consortium for Parasitic Drug Development (CPDD); the Dengue Vaccine Initiative (DVI); Drugs for Neglected Diseases (DNDi); the European Vaccine Initiative (EVI); the Foundation for Innovative New Diagnostics (FIND); the Global Alliance for TB Drug Development (TB Alliance); the HIV Vaccines Trials Network (HVTN); the Infectious Disease Research Institute (IDRI); the Innovative Vector Control Consortium (IVCC); the International AIDS Vaccine Initiative (IAVI); the International Partnership for Microbiocides (IPM); the International Vaccine Institute (IVI); the Medicine for Malaria Venture (MMV); the Microbiocides Development Programme (MDP); One World Health (iOWH); the, Malaria Vaccine Initiative (MVI); the Meningitis Vaccine Project (MVP); the Pediatric Dengue Vaccines Initiative (PDVI); the Sabin PDPl the, South African AIDS Vaccine Initiative (SAAVI); and the Turberculosis Vaccine Initiative (TVI). To date, we have interviewed several representatives from four PDPs, two of which produce drugs (DNDI, MMV), one of which produces vaccines (MVP),) and one of which produces diagnostics (FIND).

[11] We include PDPs that are part of a larger PDP organization, (i.e. MVP and MVI are part of PATH; the Sabin PDP is part of the Sabin Vaccine Institute).

[12] Instruments such as direct grants to small and medium firms and for clinical trials in developing countries, milestone or end-prizes, purchase or procurement agreements, among others, can be complementary to the role of PDPs, and PDPs themselves can use them.

trast, PDPs are R&D organizations that have emerged to bring about innovations in an area where neither the private or public non-market institutions can or are willing to do the task alone (Chataway et al 2010).

2.4.1 History of PDPs

Members of the global public health community (such as the World Health Organization, civil society organizations and doctors) initiated PDPs as a practical means to increase R&D for neglected diseases. However, it is not evident why a new organizational innovation in the form of PDPs was needed in the context of existing organizations in global public health governance. These include public research institutions, firms (e.g. biotechnology, big pharmaceutical firms), government agencies, international organizations such as the WHO, the World Bank, UNDP, UNESCO, UNICEF and UNITAID, civil society organizations and existing networks of research collaborations. We trace the origins of PDPs and identify the gaps in existing organizational structures to which PDPs are responding to.

Some of the early PDPs were catalysed at the WHO through the Special Programme for Research and Training in Tropical Diseases (TDR) and the experience with partnerships it progressively forged in the 1980s-90s.[13] Before the TDR, there was no international framework focused on coordinating research to support infectious disease control, particularly in the developing world (UNICEF et al 2007). The role of TDR evolved in time, from a focus on strengthening research capability building in endemic countries to promoting international collaboration to increase R&D for neglected diseases. Scientists engaged in the private sector had been participating in TDR committees, but the private sector was not formally engaged in the work of TDR. In time, opportunities did arise for product development in collaboration with the industry. However, it appeared to be too costly and complex to manage and implement by TDR and outside of its man-

[13] The WHO is the leading directing and coordinating authority for health within the United Nations system. The WHO TDR program, in existence since 1975, is co-sponsored by UNICEF, UNDP and the World Bank. The aim of the program was to intensify research on major tropical parasitic diseases (, taking into consideration that such activities should be carried out mainly in endemic countries),, define the research priorities, extend cooperation with national institutions and other governmental and non-governmental organizations in regard to the coordination of research in this field, and mobilize extra-budgetary resources for scaling up these objectives (WHA 27.52). The TDR was set up mainly as a partnership between public donors, co-sponsors and endemic country governments represented in an independent board-type structure. (UNICEF et al 2007).

date. With this in mind, the idea of creating independent, disease-focused organizations appeared as an avenue to speed up R&D and the delivery of new medical products to meet health needs.

TDR assisted in the creation various PDPs since 1999,[14] while other PDPs were created independently.[15] Non-profit philanthropic foundations, such as the Rockefeller Foundation, have played an active role in cultivating PDPs. The establishment of the Gates Foundation by Bill and Melinda Gates in 2000 gave a big push to PDPs as a new source of available funding. PDPs have also surged in the context of the process of "vertical dis-integration" in the pharmaceutical industry (Cockburn 2004).

2.4.2 PDPs in medical product innovation ecosystems

PDPs can be understood as functioning in the context of health innovation ecosystems (Papaioannou et al 2009) that reach beyond national boundaries. The structure of PDPs is shaped, and in turn, can shape the ecosystem in which they operate. Our context for analysis is therefore the broader ecosystem (rather than the industry), which includes the community of organizations (e.g. suppliers, sources of knowledge), institutions (i.e. regulatory authorities, government bodies), and individuals (e.g. managers, policy-makers in disease-endemic countries, patients) that influence PDPs. The ecosystem is composed of multiple players involved in the production and dissemination of drugs, vaccines and diagnostics for neglected diseases, and is influenced by external factors relating to public policy, financing, regulation, intellectual property, human resources and infrastructure, and markets.

The function of the ecosystem can be guided by principles for medical product innovation that respond to health needs. An expert commission under the auspices of the World Health Assembly advances the following principles (World Health Organization 2006):

1) *Availability:* new product development and adequate supply (quantity) of product.

2) *Acceptability:* usability and appropriateness of the product tailored to specific needs.

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[14] In 1999, the Malaria for Vaccines Venture (MMV) was created. In 2000, the Global Alliance for TB Drug Development (TB Alliance) was established. In 2003, the Drugs for Neglected Diseases initiative (DNDi) was created as a joint initiative of Médecins Sans Frontiers, TDR and representatives of disease-endemic countries. In 2003, the Foundation for Innovative New Diagnostics (FIND) was also established.

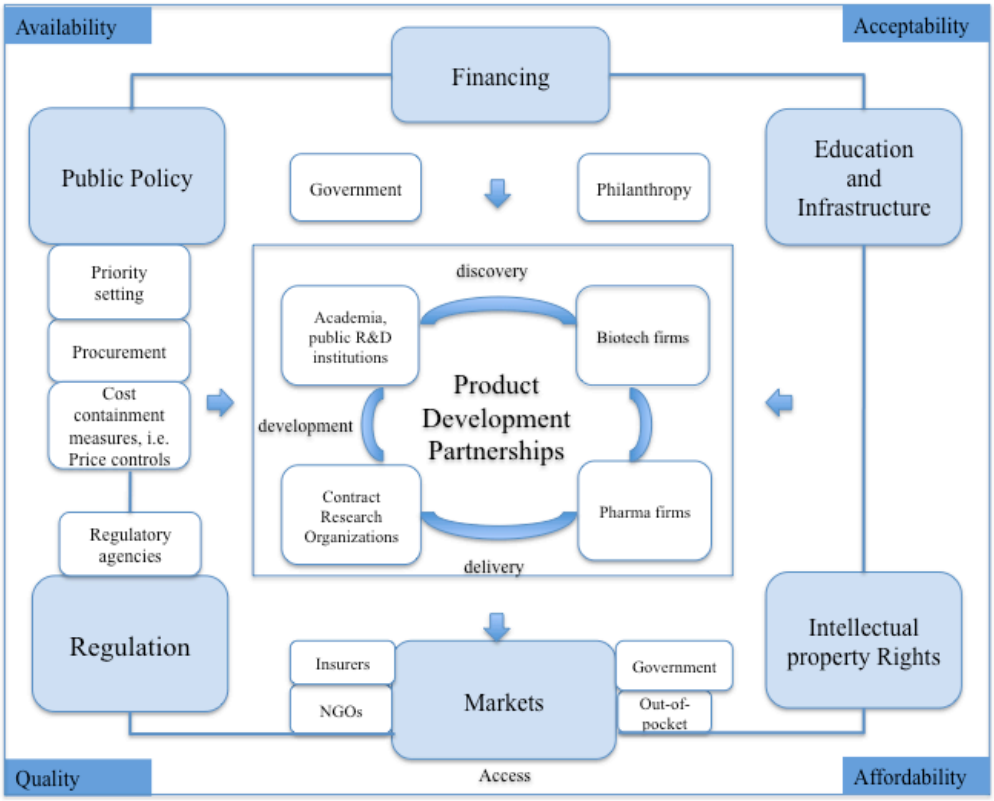
[15] In 1993, the Infectious Disease Research Institute (IDRI) was created as a non-profit research institute.

3) *Quality:* product effectiveness, standards for carrying out testing and clinical trials.

4) *Affordability:* ensuring the financing of product development and procurement, affordable prices.

Figure 1 depicts the innovation ecosystem under which PDPs operate and the principles that we consider should guide medical product development.

Figure 1. PDPs in the Medical Product Innovation Ecosystem*



Sources: Morel 2005, WHO 2006 (our elaboration)

2.4.3 PDPs as system integrators

The characteristics of PDP organizational design that differentiate them from collaborative bilateral or multilateral networks on R&D for neglected diseases, public institutions and pharmaceutical firms with R&D capacity include the following:

(i) They are established as non–profit entities that guarantee them independence and no shareholder expectations of growth and revenue maximization motives.

(ii) Their objective is to develop new medical products that can have a public health impact (specialized, access core to their mission).)

(iii) Their focus is on developing "system integration" capabilities to engage and leverage diverse resources and capabilities of various actors in the R&D chain.

(iv) They have in-house capabilities to manage a portfolio of R&D projects.

(v) External partners often undertake the R&D activities, though some have in-house R&D capacity.

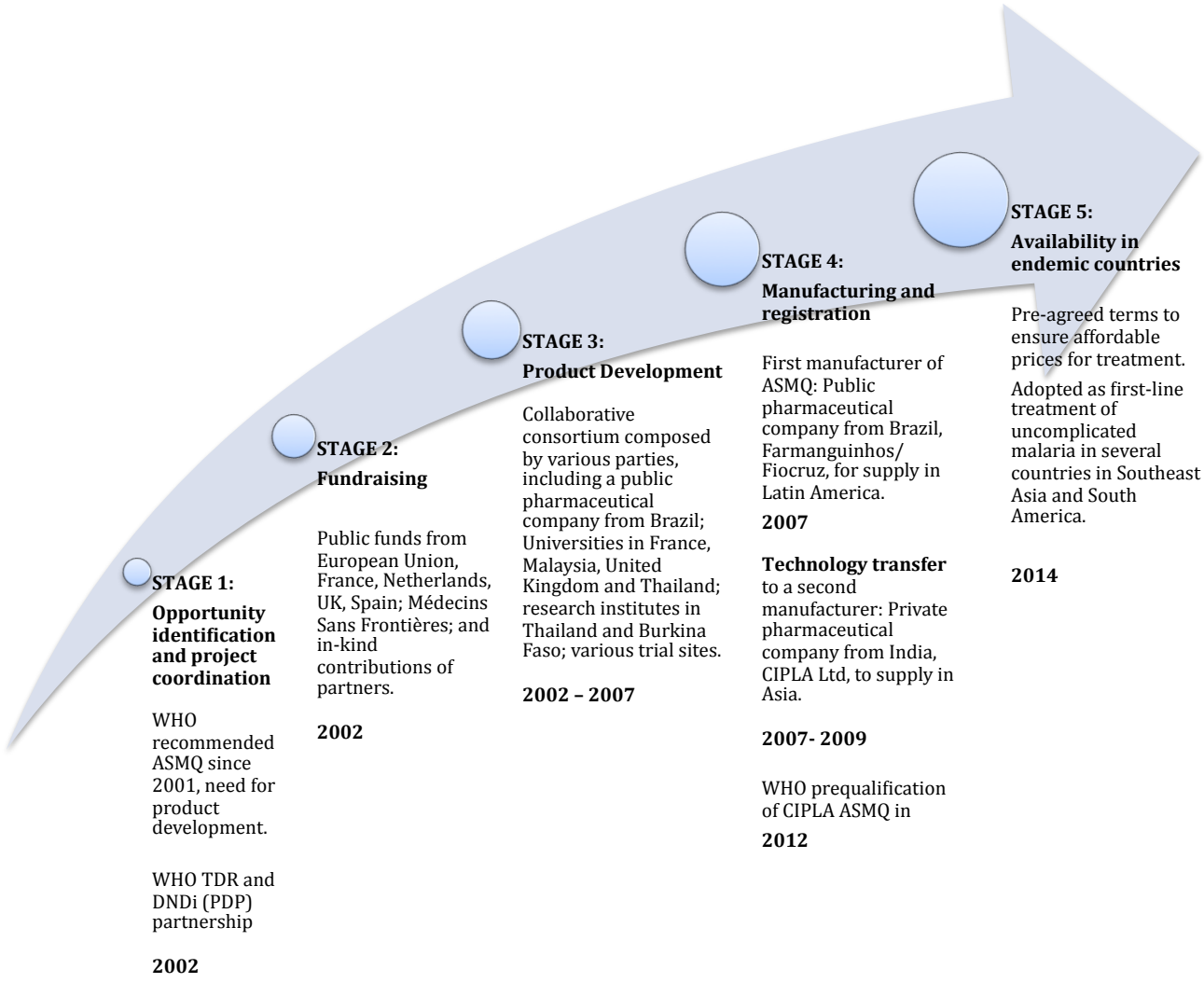
PDPs are able to operate on a not-for-profit model, provided that they can receive sufficient funding for their R&D projects and operations. A fundamental element of the PDP is thus to attract funds for donors. For public and philanthropic donors, returns to investment are measured differently than in the case of shareholders in the pharmaceutical industry R&D model. As such, philanthropic and public donors do not exert the same pressure as shareholders and venture capitalists do on for-profit firms in terms of maximizing profit. Donors are interested in the end result of PDPs in terms of medical products developed to address unmet health needs.

Funding is also a central enabling factor for R&D collaboration that takes place through PDPs. It allows PDPs to make propositions attractive to partners and reduces their risk (cost) of engagement. PDP financing is channelled to pay for services (e.g. academia, contract research organizations in clinical trials), and reduces the costs of product development for the industry involved in R&D, with clinical trials, manufacturing and registration being the largest cost factors. As described by Chataway et al 2007, PDPs can play both the role of integrator and broker among various private and public sector actors. In the innovation ecosystem, PDPs play the role of "system integrator," which can involve actors at any stage of the R&D chain, from discovery all the way to implementation and delivery.

For most PDPs, the capabilities/assets for R&D (such as financial resources, vaccine/drug discovery, development, manufacturing, distribution) do not reside with the PDP itself. Accordingly, the main avenue by which PDPs create an R&D resource base is via collaboration. PDPs search, select and draw in these capabilities/assets from external sources, including academia, pharmaceutical firms, biotech firms, contract research organizations, public and philanthropic organizations. As

example of product development through PDPs, in Figure 2 we report the case of the development of a new anti-malaria drug. The project was led by DNDi with the collaboration of TDR.

Figure 2. An example of how PDPs work: The case of the development of a fixed –dose combination of existing anti-malaria drugs, artesunate (AS) and mefloquine (MQ), for Latin America and Southeast Asia



Source: http://dndi.org/treatments/asmq/partnership.html and Wells et al 2013 (our elaboration).

Traditionally large pharmaceutical companies are rarely inclined to share knowledge outside the firm, although outsourcing research activities, mergers and acquisitions and in-licensing compounds from biotechnology firms are increasing trends (Schuhmacher et al 2013). It appears paradoxical that pharmaceutical firms are willing to engage in PDP-led R&D projects when they are usually locked into searching for the next blockbuster product (Cockburn, 2006). According to economic theory, partnerships between large pharmaceutical firms and PDPs in the form of R&D re-

source sharing for neglected diseases by for-profit companies, constrained by shareholders' values, should not take place. However, through PDPs, such partnerships do, in fact, result. The private sector lacks interest in solely undertaking the range of R&D activities for medical product development on neglected diseases. Yet, within in the PDP framework, it appears that the private sector can be induced into collaboration if costs and risks are reduced and there are other drivers, such as a boost to public relations. By working with PDPs, pharmaceutical firms can still protect shareholder value while sharing access to research tools and technology, and undertaking manufacturing and distributing final products with reduced risks and most costs covered.

For projects in the discovery phase, PDPs tap into the skills in academia, biotech and large pharmaceutical firms as knowledge sources, negotiating access for compound libraries[16], know-how and compound screening capabilities. PDPs often engage pharmaceutical firms for manufacturing, where the latter provide in-kind contributions, such as infrastructure and personnel time, which aid in low-cost production.

Academia and other public research institutions generally do not have the full range of necessary resources, capabilities or assets to undertake medical product R&D, even though there is a resolve to address unmet health needs. Public sector institutions involved in R&D are usually focused on discovery and creating knowledge (upstream) and translational research, while the industry is more focused on product development (downstream) and submissions for regulatory approvals, manufacturing and scaling, distribution and sales. For a PDP, the measure of success is not only product development. As noted in the previous section, the aim is to develop new medical products that are effective, high quality, acceptable to the target group, and available at an affordable price. Accordingly, a number of PDPs have agreed to a common definition of "access" as referring to a coordinated set of activities needed to ensure that the products developed will ultimately have an equitable public health impact (Brooks et al 2010). Moreover, many PDPs establish "access" policies. A PDP access policy may include defining upfront the contours of a technology that is appropriate and has affordable resource-limited settings. Generally the target product profile for each R&D project is developed taking into account the unmet need, the disease profile, and the local environment (including the regulatory framework, purchasing power) in which the product would be delivered. They may also define a product design and set benchmarks for product

[16] Access to the chemical compound collections of pharmaceutical firms is very important. However, the firms themselves caution that the existing chemical diversity in pharmaceutical firms in search of new drugs is limited (Payne et al. Nature Reviews Drug Discovery, 2007). The portfolio of several PDPs includes projects for radical innovations (i.e.,. the discovery of new chemical entities).

manufacturing cost and the final price. The PDP product profiling helps clarify expectations for all partners and subcontractors in R&D projects.

Most PDPs pick up opportunities for projects based on dormant or discontinued research elsewhere that can be applied to neglected diseases. PDPs producing drugs have generally focused on developing repurposed products rather than NCEs (Pedrique 2013). In the area of vaccines, this is also the case. For instance, the most clinically advanced malaria vaccine candidate to date RTSS is being developed by the pharmaceutical firm GlaxoSmithKline (GZK), the PDP Malaria Vaccines Initiative (MVI) and PATH.[17] RTSS is not a new vaccine candidate. Scientists at GSK, in collaboration with a US Department of Defence biomedical research laboratory, created the vaccine in 1987. The pricing arrangement announced for the RTSS 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 (MVI 2013).

PDPs generally also aim to keep down the costs of R&D. While PDPs have to cover the costs of the product development and take into account the costs of product delivery (including registration costs), PDPs are aware that they need to stay as close as possible to the marginal costs of production to meet their access goals. PDPs are able to channel most of their resources to pure R&D activities (in addition to R&D portfolio management and advocacy for funding),) as compared to marketing (to promote sales),) which may command a larger budget for research in large pharmaceutical firms.

In negotiating the terms of engagement with partners at the development stage, PDPs need to carefully evaluate the access considerations in negotiating the price of manufacturing and distribution by a partner, as well as the acceptability for a partner to manufacture and distribute drugs in disease-endemic countries with long-term sustainability, at an “at-cost” or “no profit, no loss” basis. PDPs need project managers with good market knowledge and negotiation skills. PDPs can leverage the fact that commercial incentives do exist for certain neglected diseases, such as HIV/AIDS, malaria and tuberculosis (TB), which are prevalent in both developed and developing countries. PDPs can also identify target products that may have potential commercial markets in the private sector in disease-endemic countries, where manufacturers can make a margin on sales, and may leverage this incentive in order to obtain better terms (e.g. lower production cost and

[17] The results of phase III trials of the vaccine’s capacity have shown approximately a 50% percent success rate.

final sale price) in the public sector within disease-endemic countries.[18] PDPs can assist in bringing overall costs down by leading and financing the registration processes or by finding other partners for this purpose.

2.4.4 Governance of PDPs

PDPs maintain governance independence as self-established entities, though they depend on external financing. The management of R&D projects involves partners that are vertically disintegrated, and this internal management structure brings flexibility to PDPs in their decision-making. There is little pressure for PDPs to expand, as is the case with pharmaceutical firms that often face pressure to undertake mergers and acquisitions in order to keep up with the growth expectations of shareholders. Pressure to contract in size is more likely, in case of reduced funds.

In the PDP analysis, it makes sense to give attention to the role of R&D managers and managerial processes (Technical Advisory Body-Board-Managers), as PDPs' main job is to build and manage R&D project portfolios. Managers play the critical role of coordinating and overseeing partners' separate tasks and building synergies, as most PDPs' R&D activities are carried out outside of the PDP. The leadership in terms of decision-making remains within PDPs, while in most PDPs, the R&D activities are outsourced to partners, which have been described as "virtual" R&D organizations (Grace 2006, 2010). PDPs build specialized capabilities in project portfolio management by focusing on a single type of medical product and a single disease or a core set of diseases. Such a framework endows PDPs with disease-type experience that biotechnology or pharmaceutical firms rarely have.

The entrepreneurial aspect of PDPs deserves to be highlighted. PDPs are built by individuals or groups of individuals with an idea (purpose to drive R&D into neglected diseases), who identify opportunities within the ecosystem (new sources of philanthropic financing, growing openness to R&D collaboration in the pharmaceutical sector) and design an organizational form under which it

[18] A case example is the combination drug ASAQ developed by DNDi in partnership with Sanofi. It is now registered in over 30 sub-Saharan countries and India, and is prequalified by WHO. DNDi developed ASAQ in collaboration with Sanofi and other partners; it claimed a patent and then licensed it out to Sanofi for African and other developing countries. Under the DNDi/Sanofi agreement, Sanofi has committed to supply the public sector in endemic countries at a no-profit-no-loss maximum price of US$ 1. In the private sector, Sanofi is free to sell at market price and pays a royalty back to DNDi, which is reinvested in additional studies. DNDi and Sanofi agreed not to file any new patents; as a result, the drug can be freely produced and distributed by any other pharmaceutical company in the world. DNDi is currently facilitating technology transfer to ensure the production of ASAQ by an African manufacturer.

may be possible to assemble the resources/capabilities needed to carry out R&D, taking into account the specificities of the market for new products for neglected diseases. The organizational and managerial processes in PDPs include selecting targets for R&D projects and management of the project portfolio, including the various alliances/contractors. Managers, advised by boards and technical bodies have a central role in making operational and strategic decisions to identify complementarities and select and align internal and external assets for developing target products, and then in engaging external partners where necessary to access the necessary assets and capabilities. This "asset orchestration" (Teece 2012) is a core capability that PDPs need to build and continuously strengthen.

Experienced project managers are core assets of PDPs. Once disease and target product profiles are set by the PDP (taking into account scientific, financing and access considerations), project managers source, negotiate, and manage partnerships with public and private sector participants. They drive discovery projects; select which promising candidates to advance to trials or products to advance through the pipeline or projects to terminate. In managing risk, the considerations for PDPs are similar as in pharmaceutical firms. The overall measure of success in advancing the R&D portfolio is the number of product approvals that meet the target product profile, with few project terminations. PDPs work on the basis of attrition rates and pre-established milestones and timelines. Evaluation of PDP effectiveness is made through project portfolio management, based on the initial plan. This is the same overall process as in a pharmaceutical or biotech company. PDPs have generally adopted "private sector" managerial methods for their work. They are not-for profit, but nevertheless aim to operate efficiently. Donors/funders also monitor PDP performance and may require measures of cost-effectiveness and public health impact, although donor requirements are not harmonized, nor are the processes or measures harmonized among PDPs.

PDPs generally have a small, core team of staff with public health and industry experience, whose work is overseen by a Board. PDPs try to compensate for their limited internal capacity in terms of their own staff (limited experience in project management from discovery up to development, and delivery) by engaging outside expertise in an advisory manner (similar to the WHO TDR model). External expert advisory bodies provide additional technical and scientific expertise. Boards are influential in the PDP overall strategy and portfolio design, but project management tends to be an activity left to the project managers that are the core PDP staff. The technical staff members in PDPs also receive advice from technical advisory committees that are composed of experts in medical product development and related areas. The Board membership mixes skill and experi-

ence from the public and private sector. The incentives for members of the Board are not monetary.

2.4.5 PDP capabilities

We now identify several types of capabilities that PDPs in their "systems integrator" role need to build and maintain. PDPs need strong organizational capabilities to detect and obtain the necessary resources and capabilities, which may reside in multiple sources. Once these resources and capabilities are obtained, PDPs t bring them together into a single R&D project designed to meet its health needs, as well as make key decisions throughout the project lifetime, such as whether to terminate a project and product pricing. PDPs also require strategic planning capacity, particularly at the initial stage in building the target product profile and in making strategic decisions thereafter, for instance, on the choice of technology and partners. Staff and governance structure is a key source for building the necessary organizational capabilities. Knowledge capabilities required include knowledge of the diseases, context and demand, knowledge of medical product R&D at all stages and requirements for product approval. PDPs also require negotiation, strategy and marketing capabilities in relation to contracting services, building R&D collaborations, and mobilizing funding and broader public support for their activities. The financial capability of PDPs is directly related to their ability to detect and mobilize external funding sources. Communication and relational capabilities are also central in the PDP structure, which requires frequent interaction with donors, endemic-country governments, and partners, among others. Finally, PDPs require the capacity to adapt to changes in their environment, such as flux in the burden of diseases, financial resources, government priorities and the entrance or exit of other initiatives on medical product innovation for neglected diseases.

2.5 PDPs : Variety within the landscape

While PDPs share common characteristics, there are important differences among PDPs. PDPs vary in their legal form, scope, internal structure and how they make strategic choices. Table 1 describes common PDP characteristics and differences.

Table 1. PDP Common Characteristics and Differences

PDP Common Characteristics	*PDP Differences*
Non-profit institutions	Legal form: stand-alone versus part of another organization, permanent versus temporary
The objective is product development of medicines, diagnostics, vaccines and biologicals for neglected diseases.	Scope: disease and geographical coverage, type of medical products developed, involvement in implementation phase
Priority-setting is driven by medical needs: products developed need to be affordable and adequate to the local context to facilitate uptake. Define the target product profile. Requires low cost of product manufacturing and selling price.	Internal structure: size of staff and roles, outsourced versus in-house R&D capacity, governance model, external advisory support
The public health goal and R&D objective of PDPs drive their strategic choices (e.g. priority setting, governance and sources of financing).	Strategic choices: IP policy, partner selection and type of relationship, transfer of technology to developing countries, capacity building for developing countries
Collaborative R&D model: most PDPs have little or no in-house R&D activities, work with a diversity of partners from the public and private sectors. Managing the collaborations is the key task of a small core number of in-house staff in PDPs.	
Internal structure: core staff, Board, advisory committee	
Funding from philanthropic and public sources	

2.5.1 Legal form

While PDPs are all non-profit institutions, they vary in their specific legal form. Most PDPs are stand-alone entities, yet a few are part of a larger organization (e.g. MVP and MVI are part of PATH, the Sabin PDP is part of the Sabin Vaccine Institute). Likewise, most PDPs are registered as non-governmental organizations (i.e., IAVI, the TB Alliance), while some are recognized as international organizations (i.e., DNDi, FIND, MMV in Switzerland). PDPs are generally created as a permanent institution, but some PDPs, particularly those that are a project of a larger institution, can be of a temporary nature, to complete a particular goal (e.g. develop a medical product for a specific disease target) and are discontinued thereafter (i.e., MDP has terminated its activities since 2009, although the founding organizations continue to carry out similar work).

2.5.2 Scope

PDPs vary in scope, including the terms of their disease coverage, geographical area for which they target their medical products, the type of medical product to develop (medicine, microbiocide, vaccine or diagnostic), and the level of involvement of the PDP in activities during the implementation phase**.**

The variance in the disease coverage of PDPs is presented in Table 10 in the Appendix. Most PDPs focus on a single disease, although some PDPs cover up to 6 diseases. Malaria is the disease most covered. The profile of each disease presents specific challenges for medical product development through the PDP model. For example, while most neglected diseases affect particular geographical regions or countries, some diseases such as HIV/AIDS, malaria and TB have a broader geographical reach in terms of disease burden. This, in turn, creates to some extent market incentives for private partners (i.e., populations in developed countries travelling to endemic-ridden areas in developing countries for tourism or military missions).

In Table 2, PDPs are classified in accordance with the type of medical product they aim to develop. We identified 15 PDPs for vaccines, 4 PDPs for new medicines, 4 PDPs for microbiocides, and 2 PDPs for diagnostics.

Table 2. Type of Medical Product by PDP

	Drug	Vaccine	Vector control pro-	Mi	Di
AERAS		X			
MMV	X				
DVI		X			
EVI		X			
IVCC			X		
IAVI		X			
OWH	X	X			X
IVI		X			
MVI		X			
MVP		X			
PDVI		X			
Sabin PDP		X			
SAAVI		X			
TBVI		X			
DNDi	X				
CPDD	X				
TB Alliance	X				
IDRI	X	X			X
CONRAD				X	
HVTN		X			
IPM				X	
MDP				X	
FIND					X
Total	6	14	1	3	3

Disease profiles also vary in their mortality rates and incidence. Moreover, the scientific and knowledge challenges vary among diseases (i.e., whether any products are currently available for prevention/treatment or cure).

PDPs also vary in their level of involvement in the late stage development process. While all PDPs work from the point of discovery to product development, some PDPs stop at the point where the product is developed, while others continue to follow up implementation activities, including as-

sisting in product pre-qualification by WHO, national registration and uptake and delivery in endemic countries.

2.5.3 Internal structure

The size of core staff of PDPs varies largely in respect to the size of the PDPs' R&D portfolio and disease coverage. Some PDPs that have a large portfolio have operations in more than one country or location. We also find some variance in the specific roles of the staff, Board and advisory committees and their relationships with each other and partners involved in R&D projects.

2.5.4 Strategic choices

There is a significant variance in the strategic choices of PDPs in terms of the way R&D is undertaken, how the portfolio is managed, and in particular, the selection of and agreements with partners. While most PDPs do not carry out R&D activities in-house, some PDPs do undertake their own research, as in the case of IDRI and AERAS. PDPs also vary significantly in the way they manage their R&D project portfolios.

As noted in the previous section, some PDPs define upfront target product profiles for the R&D project. However, some PDPs adopt a more flexible approach to determine product profiles, for example, opting to define a pricing strategy for the new medical product at a later stage. PDPs may also vary as to whether they have a defined "access" policy (guidelines as to how to ensure that the new medical product will be available to those in need). Most PDPs have some basic principles on ensuring access that guide negotiations for access to knowledge (compounds for screening), low cost of production from industry partners and royalty-free licenses, at least for endemic countries.

In some PDPs, negotiations and relationships with partners are guided by broader policies, in areas such as intellectual property (IP). An IP policy serves in some PDPs to inform their strategy for the management of intellectual property rights (IPRs), in particular to ensure that IPRs do not create obstacles for the PDP to access know-how and assets, affordability of new products, and follow-on R&D. However, in some PDPs, decisions on IP management are taken on a case-by-case basis, which is viewed as providing the PDP with greater flexibility. Overall, there is significant variance in PDP practices on IP. Some PDPs define at the outset that IP should generally not be sought for any

product developed, while others define that the partner can claim or share with the PDP the IP from a potential product along with licensing terms (e.g. non-exclusive or exclusive terms of licenses for pre-existing IP or new products developed). PDPs may also have particular policies concerning the level of control that the PDP, partner or funder may have over the R&D project (decision-making). PDPs generally face greater pressure from partners to have a stake in decision-making when the financial input of the partner is substantial. PDPs may also have particular policies concerning funding sources (such as specifying a minimum percentage of the PDP budget that should be covered by public funding as opposed to private)PDPs also vary in the extent to which they consider capacity building and the transfer of technology to developing countries a part of their mission. For example, DNDi includes these activities as a part of its mandate. In South Africa, SAAVI is linked to the national Medical Research Council, and its work includes programs to support community involvement and education interventions in relation to HIV issues.

There are numerous projects that include the transfer of technology to developing countries, such as the involvement of the firm Zenufa, based in Tanzania, as a second manufacturer of ASAQ -- a DNDi product. Another example is the meningitis vaccine MenAfriVac, manufactured by the Serum Institute of India (SILL) Ltd, Pune, India –a product of MVP. The decision on whether to go with a manufacturer in a developed country, or a clinical research organization from a developing country is also a strategic one. Considerations include the cost of production and knowledge of the disease and local context to promote affordability and uptake of the medical product in endemic countries.

2.6 Discussion

We have shown so far that PDPs contribute to increasing R&D in order to address the lack of new medical products for neglected diseases. We have also explained how PDPs function within the broader context of medical product innovation ecosystems, and how PDPs are able to bring about R&D collaboration. We have also identified the core capabilities that PDPs need to build and strengthen in playing the role of “system integrator” to stimulate R&D in neglected diseases. Furthermore, we analysed the variety among the PDP landscape. In this section, we discuss the potential shortcomings of the PDP organizational form and current operation.

2.6.1 Constraints on the determinants of R&D productivity

PDPs appear to still have limited R&D capabilities. In the case of pharmaceuticals, to date PDPs have focused to a substantial extent on "low-hanging fruit": existing drugs being evaluated for new indications, new formulations of existing drugs, novel fixed-dose combinations, but not NCEs. PDPs have yet to prove whether they can develop NCEs, though there are a number of NCE projects in late-stage clinical trials. NCEs are riskier to invent than finding new uses for existing drugs or new formulations. The latter can be developed in a shorter timeframe, and thus can be delivered to those in need in shorter timeframe. Nevertheless, the discovery of new NCEs will be needed to achieve substantial improvements in terms of therapeutic benefits over existing drugs. Transaction costs and coordination costs are higher and more complex. Mobilizing sufficient financing for projects on NCEs is a major challenge.

Project managers in PDPs need to be highly skilled in order to accomplish the range of activities they may be entrusted to do, or if these activities are separated among project managers (by R&D phase or activity), they will need to be highly coordinated among them, (i.e., scientific expertise, evaluating licensing opportunities, designing appropriate clinical trials).

The size of PDPs may vary, though generally they are small organizations. The empirical evidence on the relationship between firm size and innovation is inconsistent (Cohen 2010). Some empirical literature finds that in the pharmaceutical industry, size confers an advantage. Henderson and Cockburn found that discoveries in larger pharmaceutical firms are more productive, deriving from economies of scope and scale (Henderson and Cockburn 1996). Yet in drug development, large firms have the advantage of scope, rather than returns to scale (Cockburn and Henderson 2001). However, small firms, such as biotechnology firms, can be highly innovative. The share of NCEs attributable to small biotechnology and pharmaceutical firms has increased to nearly 70% since 1980 (Munos 2009). Moreover, the large scale of R&D portfolios in large pharmaceutical firms and trends in growth via mergers and acquisitions have not lead to their increased innovativeness in terms of newly approved NCEs.

PDPs with small project portfolios may have a perverse incentive to cling onto projects that should otherwise be terminated. There is evidence that single-product early stage firms are more reluc-

tant to abandon the development of their only viable drug candidates, in contrast to firms with multiple products in development (Guedj and Scharfstein 2004).

2.6.2 Constraints on financing and priority setting

Governments of disease-endemic countries, global health organizations (particularly WHO) and, public and philanthropic donors lack coordinated R&D priority agendas and funding efforts, based on the global burden of diseases. Currently activities are highly disjoined.[19] This lack of coordination is also reflected among PDPs.

PDPs, as has been pointed out with respect to other multi-stakeholder institutions in global health, derive their legitimacy from their effectiveness in improving specifically defined health outputs and outcomes, in contrast to traditional multilateral agencies, which derive legitimacy from multi-government representation and deliberation (Sridhar, 2012). In PDPs, donors decide on the priority areas for funding, the conditions attached to fund disbursements, instruments for control, transparency requirements, and so forth. These requirements are not harmonized among PDPs, nor are they made public. The risk is that the priorities of governments, particularly from endemic-disease countries, do not match those of the donor; therefore, the PDPs' R&D efforts may deliver products that will not find entry in disease-endemic countries. Currently there is no assurance that the current portfolio of PDPs' R&D projects will match the expectations of disease-endemic countries.

PDPs maintain close relationships with partners in collaborative R&D schemes. The interests and priorities of various partners, public and private, can be at odds. The PDP has the role of neutrally managing these tensions, but it is not exempt from influence. Hence, PDP access and other related policies are critically important. Not all PDPs openly disclose their policies for the establishment of partnerships. None disclose the details of the deals made. While this is standard practice in the pharmaceutical industry, in pursuing the public health objectives of PDPs in the non-profit framework, greater transparency should be expected.

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[19] A WHO expert working group (CEWG) proposed a binding R&D treaty to improve priority-setting based on public health needs, and to promote increased government financing for R&D and coordination among public and private R&D (CEWG 2012). There are proposals by governments, civil societies, and PDPs for the establishment of a global R&D framework that monitors, coordinates, and finances medical innovations for neglected populations, in the form of a new R&D treaty (DNDi and MSF 2012) to establish a Global Health R&D Observatory within WHO.

PDPs, as independent entities, could use added oversight from the global public health community. Currently some level of oversight is exerted only privately by funders. WHO could provide additional leadership in establishing priority areas for R&D in neglected diseases and could coordinate with other new multi-stakeholder institutions that assist in the purchasing and disbursement of new medical products such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the GAVI Alliance. However, the ability of countries to align their priorities for programs with the budget at WHO is currently restricted. Member States approve and decide on the use of only the portion of the budget that is financed by Member State contributions (about 25% of total funding), while donors decide on the use of extra-budgetary (voluntary) funding (over 80% of total funding) from State and non-State actors.[20]

Donors, especially philanthropic foundations, are also not responsive to any broader global health community. Their legitimacy, as in the case of PDPs, rests in the effectiveness of their interventions, but is delinked from any accountability to governments. With their amount of resources, they are able to exert enormous influence on global health policies. The interviews we conducted point out that PDPs are not always clear in terms of who is setting the priorities for the PDP. Moreover, various interests are aligned, whether it is the funder, (i.e., with the Bill and Melinda Gates Foundation being the largest philanthropic donor), the Board, the pharmaceutical industry partner, or the government of endemic-disease countries. When a representative of a PDP was interviewed, we were told, "When Gates says that we should increase efforts for vaccines, we know that the risk for PDPs not in the vaccine field is real". There could be potential conflicts of interests in the Board, for example, when an active pharmaceutical company representative or funder (i.e. Gates Foundation, Médecins Sans Frontiers) is on the Board. PDPs do not seem to have a clear strategy on how to tackle the issues. Some PDPs want to maintain independence and give assurance of being a neutral catalyser for R&D, while others consider it to be of great importance to have key partners represented on the Board.

PDP financing is also not assured on a long-time horizon. PDPs are highly vulnerable to fluctuations in financing, especially at times of financial downturns affecting governments and donors. Public and donor financing to PDPs are reported to have decreased in light of the recent economic downturn since 2008, down US$128.7 million (G-Finder 2012). Furthermore, PDPs must invest considerable resources to be used in fundraising and public relations. They have to undertake market-

[20] See the WHO document A66/48, WHO Reform, Financing of WHO, Sixty-Sixth World Health Assembly, Provisional Agenda Item 11, 13 May 2013.

ing and advocacy activities to attract new funding. PDPs' R&D portfolios are mostly in the early stages (development, early clinical stages), with important exceptions. As projects progress to larger clinical trials, the costs will likely increase significantly, together with total funding needs. There may not be adequate cost estimations of the total funds needed for completion. Already some PDPs are struggling to ensure the estimated funding required for their phase III projects (i.e., as is the. case with DNDi projections).

Some PDPs have been experimenting with alternative means to raise financing, in addition to advocating for increased resource allocations from the global health community. For example, IDRI created three for-profit start-ups (biotechnology companies) as a means to continue financing for its non-profit arm, including licensing vaccine adjuvants to pharmaceutical firms for developed country markets that were originally developed for neglected diseases (Nature Biotechnology 2009). One problem identified is that PDPs cannot attract venture capital or some types of grants (e.g. small business grants in the US) that are available to small innovative firms, but not to non-profits. However, the relationship between non-profit and for-profit arms of PDPs is likely to increase tensions with respect to the public interest mission of PDPs.

2.6.3 Constraints of access and delivery

The PDP setup creates tensions between incentives to R&D and access goals. In practice, managing an agenda of R&D plus access is complex. A case example is defining the product price and IPR policy. In cases where the market is too small to stimulate competition, products will need to be supplied at cost, or at a price corresponding to a small margin above the lowest manufacturing costs to ensure sustainability of production. Yet, due to asymmetric information, PDPs can be paying higher than "at cost" to partners, who may also seek IPR protection for the new medical products, in particular, for diseases that have some commercial market (i.e. HIV/AIDS, malaria, tuberculosis, meningitis).

PDPs also face challenges of ensuring that end users can access products once they are developed. Introducing new tools for various indications has often been associated with a significant delay between global availability and local adoption. Donors are funding product development, but not product delivery. The capacity to conduct research to support and sustain public health initiatives

in developing countries remains weak, which is a barrier to the long-term availability of existing products.

2.6.4 Constraints of contracting and coordination problems

The disintegrated R&D structure of the majority of PDPs raises contracting problems and transaction costs, as compared to centralized vertically integrated R&D within a single organization (Cockburn 2005).

Problems of asymmetric information exist in contracting with partners. Academic researchers may be better aware of the true value of their research, and may contract research organizations (CROs) about the costs of clinical trials, and pharmaceutical firms about the cost of manufacturing and distribution. Moral hazard may occur, in particular in manufacturing, given that PDPs cover most of the costs; therefore, the firm involved is more likely to take risks. The contractual terms of PDP collaborations are not disclosed. Non-disclosure of contractual terms makes it more difficult for PDPs to share information, learn from each other's experience and share it with outside R&D projects. In particular, IPR terms can limit the freedom of PDPs to coordinate R&D, grant sublicenses for manufacturing and other activities with third parties.

We observe that PDPs tend to select those with whom they have previously worked. A possible explanation is incomplete information on potential partners. In doing so, opportunities for collaboration may be missed, for example, with partners from disease-endemic countries.

PDPs operate independently, with no overall coordinating entity or priority-setting public policy guidance, other than their own PDP governance structure and pursuit of their mission. The only coordinating entity, to some extent, is the Gates Foundation. As a funder of several PDPs, the Foundation sees the broader picture of PDPs' R&D projects; yet, an analysis of PDP portfolios or other initiatives to coordinate at a broader level are not disclosed to the public. PDPs may be subject to the problems that pharmaceutical firms face in pursuing the same leads to dead ends, making unnecessary efforts to replicate screening, and studies that others have already undertaken.

There can also be a lack of coordination and collaboration among PDPs, leading to unnecessary duplication of efforts, though we do not have sufficient evidence to explore the extent to which this may be affecting R&D outcomes. Competition in a non-profit economy is a topic not often

explored. In the case of PDPs, it is evident that PDPs can be competing with one another for the same select sources of funding to capture resources. The overlapping of R&D portfolios in terms of diseases or leads may not constitute a problem in itself, given the high levels of failure that can be expected in medical product development, particularly vaccines and new drugs. However, resources may be wasted, and spill-overs may be foregone by a potential lack of cooperation and sharing of information and resources among PDPs. If the sources of financing for PDPs are not assured, or if policies are not implemented by governments and funders to regulate PDP behaviour in another direction, this competitive environment can be expected to continue. However, there are indications that PDPs are working to increase coordination and collaboration amongst themselves. For example, the TB Alliance granted DNDi a royalty-free license to develop anti-TB compounds for use against other neglected diseases in the R&D portfolio of DNDi.

Sharing information among PDPs can also serve to build collective bargaining power to achieve better deals and to strengthen their future negotiating positions with partners, particularly with pharmaceutical firms. PDPs could share with one another their experiences in negotiating with partners, the terms of deals, including a better understanding of how firms define terms such as what “at cost”, “no loss”, “fully burdened manufacturing cost” and “cost plus”, which may significantly vary the cost of a PDP R&D project, and strategies for IPR management. PDPs could also work more closely in their common operations, in areas such as advocacy to donors and technology platforms to bring down costs and increase effectiveness.

2.6.5 Constraints of insufficient transparency

As independent non-profit organizations, PDPs face demands for accountability from various sources, including donors, endemic country governments, partners and end-users of the medical products that they aim to treat. They are legally accountable in terms of compliance with the health regulatory standards for new medical products in general. However, PDPs could improve their transparency and disclosure, as well as performance assessment mechanisms. PDPs and partners do not systemically nor publicly disclose all relevant scientific and clinical data that could be useful, for example, cases when clinical trials fail to avoid making the same mistakes or following the same leads. PDPs need to make the terms of their deals with partners, financial allocations and costs of their R&D projects more transparent in order to allow proper evaluation. PDPs

could increase their credibility and legitimacy by establishing governance instruments and institutional policies to reduce the risk of capture or undue influence by donors and other actors and could avoid conflicts of interests in managing their R&D portfolios. Some PDPs have established policies, for example, with respect to ensuring multiple sources of financing to avoid donor capture, and policies on access and management of IPR, but these are isolated initiatives. There is also a lack of systemic assessment of PDPs, based on a commonly agreed-upon methodology or metrics. Despite the growing amount of resources being challenged for neglected disease R&D to PDPs, there are no reliable methods or regular assessment reviews of PDP performance, as compared to other alternatives (Ridley 2004).

2.6.6 Constraints on insufficient use of capabilities in disease-endemic countries

Not all PDPs see their mission as seeking to build up the capacity of developing countries themselves and technology transfer to undertake R&D on treatments for those diseases that particularly affect disease-endemic countries. Greater R&D capacity in developing countries has many benefits, such as lower R&D costs, price of manufacturing and distribution, and increasing market competition to drive down long-term prices for medical products. In the case of the meningitis vaccine developed by the PATH Meningitis Vaccine Project (MVI), the India Serum Vaccine Institute was able to offer to manufacture the vaccine at the target price set by MVI, which would allow endemic-country governments to procure the vaccine at US$0.50 a dose. No other big vaccine manufacturer was willing to produce at this price. PDPs should seek greater collaboration with emerging economies that are increasing their role in the neglected disease landscape (So and Ruiz-Esparza 2013).

2.7 Conclusions

We have described an interesting phenomenon under the lens of economics of innovation. PDPs are a new form of pharmaceutical R&D in the area of neglected diseases. We have found evidence that PDPs are able to bring about new medical products. We did not consider the efficiency of the PDP organizational form, as compared to others. Reasons for having not carried out any efficiency analysis are various. In particular, the needed data for undertaking such an analysis were not

available, and even if the data had been obtained, the absence of counterfactual cases would have strongly limited the scope of the analysis. Moreover, the various PDPs investigated in the study are not readily comparable because they deal with different diseases and medical products; thus, the scientific and technological problems they try to solve are of different levels of complexity.

In this study, we exclusively analyse the experience of PDPs in the area of neglected diseases. Nonetheless, there is increasing academic and policy interest in exploring the potential of PDPs in other areas, such as antibiotics.[21] There is also growing interest in promoting greater collaboration and information sharing to advance drug development, particularly in the pre-competitive stage of discovery.[22]

We find that PDPs act as "system integrators" that leverage the resources and capabilities of a diverse network of public, philanthropic and private sector partnerships. PDPs are able to mobilize private firms to join R&D projects and provide in-kind contributions. By binding together and co-ordinating the activities of various firms and other organizations, the PDP integrator role is beneficial to all involved. PDPs facilitate access to the financing and exchange of knowledge; additionally, they diffuse knowledge among the groups that in turn, may also be internalized by individual participants. Public policy should encourage PDP types of activities and R&D collaborations.

Some of the constraints we found associated with PDPs are coordination problems, insufficient transparency in contractual terms with partners and the mismatch between the financing horizons of donors and the timeframe of medical product development.

The future of the PDP landscape remains uncertain. Some PDPs that have completed their activities (or whose funding has ceased) have disappeared, while others have merged into larger PDP organizations. This may be an indication that there is a need for scale and scope in PDP operations, in the context of uncertain financing. It would be useful for PDPs to increase their transparency in their internal operations, their policies on critical issues such as access and IPRs, as well as in their dealings with funders and partners. Such transparency may be forthcoming if greater oversight is done by international health organizations, for instance, the WHO, neglected disease-endemic countries and public funders. An agreement for increased global coordination of priority-setting

[21] World Health Organization 2012a.

[22] See Ekins et al. 2013. In the case of neglected diseases, openness is facilitated by the particularity that funding comes from public sources, and potential profits are nil or low. For other diseases, intellectual property and profit margins are central components of the business strategy of firms, and may be the case for academia, as well. In this context, the incentive for openness and knowledge sharing in product development is weaker, although on the whole, it would be beneficial to speed up medical product development.

for R&D and resource allocation directed at neglected diseases, for instance, through the WHO, would serve to direct the work of PDPs in a more coherent and transparent manner. According to Weder and Grubel (1993), private agents have found many ways to internalize R&D externalities and solve coordination problems that arise from the public good nature of knowledge and research. They call these solutions "Coasean institutions"," according to the principle developed by Ronald Coase that knowledge externalities induce the creation of private institutions capable of internalizing them. The institution analysed and documented in this study–the PDPs –clearly represent a new Coasean solution to this broad class of problems, including R&D and knowledge externalities, as well as coordination failures in decentralized markets for knowledge and new products.[23]

A limitation of this study is the lack of information available concerning the contractual terms of PDP collaborations with partners and processes for determining how funds are allocated to partners. This information is not publicly available, and it was not possible to collect comparable data. If such information were available, future research could evaluate the performance of PDPs, including resource allocation, selection and termination of R&D projects and the appropriateness, affordability and health impact of new medical products produced by PDPs, as compared to other sources, or alternatives to promote R&D in neglected diseases.

[23] However, as Weder and Grubel cautioned, policy has to limit the natural rent-seeking activities of private agents by establishing constraints on the cooperative agreements that take place with firms within the collaborative R&D structure (Weder and Gruber 1993). In the case where public moneys are being channelled to PDPs, policy can play a role in defining the conditions for disbursement, such that all partners work to fulfil the PDP mission and avoid potential rent-seeking, and promote greater transparency.

Chapter 3 Does Intellectual Property matter for not-for-profit innovation? The case of product development partnerships for neglected diseases

This study examines how not-for-profit medical product ventures respond to intellectual property (IP) as incentives for innovation. The specific case of an institutional experiment -Product Development Partnerships (PDPs) in the area of neglected diseases - is considered. PDPs are independent not-for-profit organizations that aim to develop new vaccines, drugs and diagnostics for diseases for which there is under-investment in R&D as compared to the socially optimum level. A survey and patent data search was conducted for the whole population of PDPs. The study finds that IP protection does not encourage the R&D activities of PDPs, though PDPs are "users" of third party intellectual property rights (IPRs) and "producers" of their own IPRs. PDPs use IP for strategic purposes to advance their not-for-profit and access mandate. This finding is consistent with previous literature pointing that IP does not act an incentive for innovation in areas where commercial markets are low or non-existent. A broader conclusion of this study is that the research on economics of IPRs should be informed by institutional analysis to deepen understanding of the variations in the value, use and impact of IPRs under different institutional settings, beyond the firm. It may also serve to better understand how the behaviours of actors in R&D (i.e. firms, universities) with regard to the exercise of the legal protections afforded by IPRs can be influenced by different institutional settings (PDPs).

3.1 Introduction

It is well known that the pharmaceutical industry actively seeks out patents and other forms of intellectual property rights (IPRs) and is opposed to weakening of intellectual property (IP) protec-

tion. In contrast, the IP practices and policies of not-for-profit R&D institutions involved in medical product development are not well understood. In general, the role of IP in the context of not-for-profit innovation is an underexplored subject.

This study explores this question by examining a specific form of not-for-profit R&D organization: product development partnerships (PDPs), specifically those involved in advancing innovation for tackling neglected diseases.[24] PDPs are independent not-for-profit organizations that aim to develop new diagnostics, vaccines and drugs for diseases that concentrate in poor countries and populations and for which there is under-investment in R&D as compared to the socially optimum level. In contrast with for-profit firms, PDPs are not motivated by economic interest but rather by the objective to bring about new medical products that are accessible to poor populations. The PDP non-profit operational model allows for the cost of R&D to be delinked from returns over product sales (in the case of firms achieved via high prices) because public and philanthropic donors directly finance R&D.

The aim this study to understand to what extent are IPRs are relevant for not-for-profit innovation by examining the case of PDPs that undertake non-profit R&D through R&D collaborations with a diversity of public and private actors. It is reasonable to expect that IPRs would be of minor relevance in the context of non-profit innovation in PDPs given their mission and operating model.

The study analyzes the role of IPRs in the context of PDPs, from two perspectives. On the one hand, it considers PDPs as potential users of IPRs to obtaining access a technology or knowledge asset of a partner or a third party that is protected by IPRs. On the other hand, PDPs are considered as potential producers of IPRs, in deciding whether to obtain IPRs for outputs developed as part of an R&D project. A survey on was undertaken covering the whole populations of PDPs to understand the IP management policies and practices of PDPs. A search was also conducted for all patents held by PDPs. Overall the study contributes to the understanding the role of IPRs under different institutional settings that support R&D and innovation.

[24] The term “neglected disease” is a used to denote diseases that have a large burden in poor populations in developing countries, but no or little burden in the developed world, and that lack effective, affordable, or easy to use diagnostics and treatments. For the purposes of this study, and following Munoz et al 2014, in this study we consider neglected diseases to include Malaria, HIV/AIDS, Tuberculosis, and the group of 17 diseases classified as such by the World Health Organization, namely buruli ulcer, chagas disease, cysticercosis, dengue, dracunculiasis, echinococcosis, endemic treponematoses, foodborne trematode infections, human african trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, rabies, schistosomiasis, soil-transmitted helminthiases (hookworm), and trachoma (WHO 2010).

The remainder of the study is organized as follows. Section 2-3 reviews the literature on intellectual property as an incentive to innovation and other uses of IPRs by firms and universities alone and in R&D collaborations. Section 4 discusses the IP approaches of PDPs. Section 5 presents the method and survey data. Section 6 discusses the results. Section y concludes.

3.2 Intellectual property and incentives for innovation

3.2.1 IPRs and innovation

The understanding of incentives for R&D and innovation is a long-standing subject in economics of innovation. Economists have mainly given attention to intellectual property as an incentive mechanism and policy response to the problem of imperfect appropriability. Intellectual property is one among several incentive mechanisms used to promote R&D and innovation. The problem of appropriability refers to the situation where innovators may not be able to fully capture the profits associated with their innovation, given the potential for unintended spillover (i.e. transmission, imitation) of the information and knowledge created through their private investment in R&D (Arrow 1962, Levin et al. 1987, Winter 2006). By limiting R&D spillovers, in theory intellectual property helps innovators to protect returns to innovation. On the other hand, R&D spillovers are an important source of technical progress (Levin 1988, Cohen 2010). An implicit assumption is that there are market drivers for innovation in the first place, which may not be the case as will be presented in this study in regards to neglected diseases.

Intellectual property is a legal system that allows the exclusion of potential users of an innovation unless they meet the terms and conditions of the holder of intellectual property rights (IPRs) over it. IPRs are exclusive rights to commercialize a protected subject - matter (i.e. creative work, mark, design, product or process invention). The IPR holder can exercise the right to gain or maintain market advantage. IPRs can take various forms, including patents, copyrights, trademarks, and trade secrets. IPRs have limited durations (for trade secrets protection lasts as long as the information is kept secret, trademarks can be renewed indefinitely, unlike patents and copyright). IPRs can be exercised, traded (sold or “rented” via a licensing contract, or otherwise transferred) or abandoned (Rockett 2010). Economics literature has given most attention to patents. A patent is granted by government with regards to an invention that may be a product or a process, when the application meets the patentability requirements and with the condition that the patent applicant

publicly disclose information of the invention, sufficiently that it can be replicated and used by others once the term of protection is expired. Trade secrets, of a different nature, may also be used to protect innovations. The secret should not have been disclosed to the public and reasonable efforts must be done to keep the information secret.

Firms can use intellectual property in deciding whether and how to protect, use or transfer knowledge assets (including tacit and codified know how, technical and organizational) for their competitive advantage.[25] Nonetheless, knowledge generated through R&D is not perfectly appropriable, nor is easily transferable, often because the knowledge is tacit.

Empirical studies point to an increased propensity of firms to patent, particularly in the United States and Europe, but are inconclusive in explaining this trend. A review of empirical studies by W.M. Cohen casts doubt on the effectiveness of intellectual property as a mechanism for appropriability (i.e. patents that are invented around) and the impact of patents on innovation (Cohen 2010). An empirical study by J. Lerner also finds that policy to strengthen patent protection has not led to increased innovation (Lerner 2009). A number of other mechanisms used as incentives for innovation include government and/or philanthropic sponsored prizes and procurement, i.e. direct subsidies, research grants or fellowships, or indirectly by employing scientists in public R&D labs or universities (David et al. 1999, Gallini & Scotchmer 2002, Stephan 2010, Hall & Lerner 2010). Economists have also pointed to defects of intellectual property as an incentive mechanism due to the deadweight loss from monopoly pricing that reduce users (i.e. those unable or not willing to pay the price of the license) and inefficiencies that are caused by "patent races". Inefficiencies are due, among other factors, to the difference that may exist between the private value of the intellectual property from the social value and imperfect sharing of information among R&D competitors (Menell & Scotchmer 2007). It has been suggested that joint ventures and other strategic alliances are a way to reduce such inefficiencies related to "patent races" (Schotchmer 2003), though empirical evidence is lacking.

[25] Firms also rely on other means of appropriability to a greater extent that or in addition to IP, such as lead-time/first-mover advantage, secrecy and complementary capabilities. See for example Cohen et al 2000.

3.2.2 The strategic use of IPRs by firms

A growing body of literature is showing that firms increasingly claim IPRs, particularly patents, to pursue a diversity of objectives, other than deriving profits from the commercialization, sale or licensing of a patented invention. In this regard, an empirical study finds that firms use patents to block rivals from patenting related inventions, to threat or protect against infringement suits, to strengthen bargaining position in negotiations with other firms for protected technology (i.e. cross-licensing), as a measure of internal performance, and the enhancement of the firm's reputation – with differences across firms and technologies (Cohen et al. 2000). Similarly, a study on the patenting behavior in the semiconductor industry finds that by building larger portfolios of IPRs firms may reduce the holdup problem posed by external patent owners and enable firms to negotiate access to external technologies on more favorable terms (Hall et al. 2001).

3.2.3 Use of IPRs in non-profit institutions

Economists have also given attention to the increased patenting and licensing by public and private universities, a trend attributed in part to changes in IP regulations. Historically, universities and public laboratories did not claim IPRs. While universities continue to receive significant public financing and play an important role in the dissemination of knowledge, legislations such as the United States Bayh-Dole Act of 1980 promote patenting by universities that restricts the dissemination of the research results and inventions from university to stimulate higher levels of university - industry interaction and technology transfer. Studies show that it is unclear what is the impact of increased university patenting and caution on negative effects of patents on inputs to future research that hinder downstream research and product development (Mowery and Sampat 2004, Geuna and Rossi 2011). As argued by Sampat with respect to the role of the United States' National Institute of Health in financing basic research, "if [publicly] funded institutions start to act too much like firms with respect to their patenting and licensing activities, this would seriously undercut the economic argument for public support, from either 'market failure' or a more heterodox perspective" (Sampat 2009). Other literature points that universities that own IPRs can foster access to medical technologies by changing licensing practices towards open licensing models (Kapczynski, 2005).

3.2.4 Use of IPRs in R&D collaborations

Existing studies on the use of IPRs in R&D collaborations examine collaborations that involve firms exclusively, or firms and universities in a single industry or across industries. One study finds that firms make strategic use of pre-existing IPRs as bargaining chips and also consider IPRs as important for protecting foreground knowledge created in the research partnership (Hertzfeld et al. 2006). Another study finds that, in first instance firms prefer to divide ownership of patents that may result from research partnerships, as opposed to sharing (co-ownership of patents), given the co-patenting creates fewer opportunities for the firm to appropriate the full value of the patent, particularly where the firms have interest in exploiting the patent in the same domain of application (Belderbos et al. 2014).

3.3 A not-for-profit approach to innovation: the case of product development partnerships in neglected diseases

3.3.1 The system integrator role of PDPs

Product Development Partnerships (PDPs) are an institutional response to private and public under-investment in R&D for neglected diseases. Both private and government financing for R&D in neglected diseases remain very low as compared to the global burden of disease (Troullier et al. 2013). Medical product innovation by the private sector is driven by market dynamics. Medical products are produced and traded as private goods. Governments however have a responsibility to protecting the right to health, by providing conditions for all the population to be healthy (OHCHR 2008). Accordingly, public health policy may dictate that medical products should be accessible to all, based on health needs and regardless of the ability to pay. PDPs combine elements of private sector approach to medical product development with broader principles for public support for R&D and provision of medical products as public goods.

For purposes of this study PDPs are defined as independent, not-for profit entities that drive R&D for new medical products in the area of neglected diseases, and function as “system integrators” that leverage the resources and capabilities of a diverse network of public, philanthropic and pri-

vate sector actors (Munoz et al. 2014). Understood in this way, PDPs are discernible from other forms of not-for-profit entities and public-private collaborations, and one-off initiatives or projects.[26] The particularity of a not-for-profit organization is that its objective is not to earn profit, but rather to serve the objectives of the organization.[27] A not-for-profit organization can be formally established as a legal entity in its own right, or informally (i.e. unregistered association). The term "not-for-profit R&D organization" is used here to refer to a formally established organization that pursues a not-for-profit objective that requires substantial amount of R&D activity. The objective of the R&D is to amplify the social value of the innovation, in contrast to for-profit R&D by firms that aim to not capture as much profit as possible from their innovation. The number of PDPs has grown in the past twenty years, covering a range of diseases and medical products.[28]

The term "partnership" is used here to refer to collaboration among two or more parties to advance an R&D project, in a broad sense (not limited to joint R&D). R&D partnerships in a not-for-profit R&D organization may involve any number of not-for-profit entities (public universities and R&D labs, private foundations), for-profit entities (i.e. firms) and government agencies. The roles individual actors in the partnerships may vary, for example government or private charitable foundation may provide financing, a university or firm may provide technology, know-how and information, background IPR, infrastructure. A partnership is distinct from a regular business practice, such as the when a not-for-profit R&D organization purchases from any public or private entity a good or service against payment at market price. Moreover, for purposes of this study it is understood that a for-profit entity is in partnership when it is voluntarily engaged in an R&D project to support the objective of which underpins the not-for-profit R&D organization (as opposed to gain profits). The common objective of an R&D collaboration under a PDP-led R&D project is to advance the non-profit public health mission of the PDP, though partners may have other specific motivations for entering the collaboration.[29] Various types of entities opt to engage in different ways for the common purpose of advancing innovation for neglected diseases.

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[26] Public – private partnerships are generally established to mobilize private sector resources to deliver essential public services or involvement in mayor projects by creating favorable market conditions that otherwise would not exist. Public – private partnerships in medical product development generally follows these same lines. In the area of neglected diseases there is generally a lack of commercial market opportunities for medical product development. There may be various forms of public-private partnerships in health, PDPs are a specific form with focused objectives on product development, see for example Galea and McKee 2014, Velasquez 2014.

[27] However, not-for-profit organizations can earn revenues to pursue their objective. They are legally exempted from income tax as profits are not distributed for personal gain of its owners/shareholders.

[28] For a detailed analysis of PDPs see Munoz et al 2014.

[29] Other studies have explored the specific motivations of entities involved in PDP R&D projects. See for example Moral et al 2005, Munoz et al 2014.

There is evidence that PDPs are playing an important role in driving new R&D and innovation in the area of neglected diseases in which medical products -medicines, vaccines, diagnostics - are lacking (Moral et al. 2005, Moral et al. 2010, Chataway et al. 2010, Pedrique et al. 2013, Munoz et al. 2014). A significant amount of collaborative R&D projects in the area of neglected diseases are taking place through PDPs.[30] These involve a diversity of public and private actors, including academic institutions, public research labs, hospitals, government health and regulatory authorities, contract research organizations, biotechnology firms and pharmaceutical companies, among others. Assuming a common mission of PDPs and partners engaged in R&D projects, one can expect that the approach to R&D collaboration under PDPs would differ from arrangements in the competitive, market-driven and profit-oriented environment of the pharmaceutical industry. Trends observed in the pharmaceutical industry highlight the competitive nature of medical product development. These include the consolidation of large firms, the decline in innovation as measured by the number of new medicines coming to the market despite strong use of IPRs, and increased use of defensive patenting strategies to extend the commercial life of their products and delay the entry of generic medicines to the market (EU Commission 2009, Comanor and Sherer 2013, Sternitzke 2013).[31] At the same time, contractual R&D partnerships and licensing is common among large pharmaceutical firms and small biotechnology firms. Empirical studies associate the growth in joint R&D agreements and licenses to the pursuit of various strategic motives, including to access financial resources, technology and know-how, to reduce cost and speed up R&D, and to reach new markets (Hagedoorn 2002, Arnold et al. 2001, Roijjakers and Hagedoorn 2006).

Private firms are generally reluctant to invest alone in R&D in neglected diseases if there is low prospect of commercial returns (Matter & Keller 2008). On the other hand, academia and small firms lack the capacity to move basic research on to translational research. The PDP approach is one way address both these problems, by taking the burden of financing R&D away from the partners involved in the R&D project, and by coordinating different actors in R&D and integrating the diverse set of capabilities into single R&D projects that are managed by expert staff in PDPs. In this

[30] The emergence and growth of PDPs in the neglected disease R&D landscape can be associated to growing concern of the public health problem and new opportunity for action in light of financial resources available, in particular from philanthropic sources (Gates Foundation). However, the scarcity and unpredictability of funds, concentration of few donors puts at risk the sustainability of PDPs in the long run.

[31] Generic medicines refer to equivalent, unpatented versions of medicines that are usually cheaper than their patent-protected counterparts.

manner, PDPs are able to de-link the cost of R&D from the price for medical products, provided there are no monopoly price distortions resulting from IPRs.

3.3.2 IP management by PDPs

There are a few studies that explore the question of how PDPs are affected by pre-existing IPRs and how they may use IPRs in pursuing their goals.[32] In this study we broadly refer to these questions as "IP management". Existing studies explore IP management policies, practices or strategies of a single or selected number PDPs, rather than the whole population of PDPs. In particular there is a lack of empirical study of the IP management policies by PDPs and the terms of IPRs in R&D deals and licenses with partners.[33]

This study aims to identify and understand the IP management policies by PDPs. In doing so, the study draws a distinction between PDPs as "users" of IPRs, and PDPs as "producers" of IPRs. The term "users" of IPRs includes instances related to obtaining access to a technology or know-how that is protected by IPRs and ensuring that the PDP or no partner in an R&D project infringes (in violation of) any pre-existing IPRs of third parties. The second is PDPs as "producers" of IPRs. This concerns the decision of a PDP whether to protect the know-how or innovations resulting from R&D projects with IPRs, whether to allow partners in an R&D project to do so, or allow for joint IPRs, and whether to buy as opposed to in-license an IPR (i.e. patent) held by a third party.

PDPs as "users" of IPRs

The term "users of IPRs" should be understood in the context of this study as obtaining authorization from the IPR-holder to use IPR-protected technology or know how or any situations where the PDP can use the IPR-protected technology or know how lawfully. An assumption of this study is that the aim of the PDP is not to access IPR per se (i.e. to build their own IP portfolios through in-licensing), but to access technology and know-how that is relevant to initiate or advance an R&D

[32] Studies include Mahoney et al 2007, Eiss et al 2007, Taubman 2010, Global Coalition for Health Research 2013.

[33] This is partly due to the fact that the terms of research agreements and licenses are generally confidential. Some individual PDPs do report publicly their IP policies that guide their IPR practices. Munoz et al 2014 emphasize that greater transparency by PDPs and partners should be encouraged the donor and public health community.

project in the PDP portfolio. In following, the study assumes that gaining rights to use to pre-existing IP held by external sources is pursued when it is necessary to kick off or advance an R&D project, or where not doing so may lead to legal action. PDPs may be either "passive" or "active" users of IPRs.

Most PDPs do not have or have limited in-house capacity (i.e. own labs, manufacturing facilities), to carry out the full range of R&D activities for medical product development. Most PDPs build their portfolio of R&D projects by defining a target product and then tapping into the various sources of knowledge for various public and private sector actors that may or may not be protected by IPR (from university, biotechnology firms, pharmaceutical firms), and coordinate and finance the participation of those actors and activities through the course of an R&D project. This means that PDPs often negotiate access (free or subject to payment) to IPR-protected technology or know-how as inputs for their R&D projects.

Where IPR is present, access to a technology/product embodying the IPR requires negotiating user rights, usually in the form of licensing.[34] Ensuring rights to use third party IPRs is critical to allow the PDP to develop and market new medical products that are accessible to the target patient group. The extent that pre-existing IPRs, particularly granted patents, can inhibit the ability of PDPs to use the needed technology or know-how may this be dependent on the terms of use that PDPs are able to negotiate with partners. Previous studies indicate that patents can pose obstacles for new product development for PDPs. This is the case where patents granted in disease-endemic developing countries and existing "patent thickets"[35] hinder new R&D and innovation by PDPs, as in the reported case of malaria and HIV vaccines (Mahoney et al. 2007, Clark et al. 2011). These studies also note that some PDPs undertake mapping and analysis of existing patents (also known as patent landscaping or patent mining) to gain information to determine the extent to which existing patents are a hindrance and also to define the options available for the PDP, such as to seek to undertake collaborative research with the patent holder, or a license. Once patents are identified, negotiating licenses may still be a very complex process, particularly in the case of patent

[34] R&D agreements are commonly done in the discovery phase. PDPs get access to the technology by the license to the IP, but not necessarily the know-how. Know-how may be added to the agreement and may be no less important than access to the technology. We may want to add some discussion on this here or elsewhere in the study to clarify that the aim of the PDP is to access technology and know how and innovate, where IP is relevant only to the extent that it may be conducive or a barrier to this goal, but it certainly is only part of the whole picture.

[35] A patent thicket refers to a set of overlapping patent rights that require that those seeking to commercialize new technology obtain licenses from multiple patentees (Shapiro 2001).

thickets, were the PDP may need to get a license from multiple patent holders to start an R&D project.

Another alternative to solve the problem of patent barriers would be for patent holders to voluntarily facilitate licenses on reasonable terms to foster innovation and repurposing of existing patented medical products for neglected diseases.[36] This is readily foreseeable given the low prospects of revenues from licenses and from enforcing patents. One way for patent holders to facilitate collaborative licensing with reduced transaction costs for the patent holders is through patent pools.[37] UNITAID started the first patent pool for drugs - The Medicines Patent Pool Initiative (MPP) – which functions since 2010 for HIV drugs (Hoen E. et al. 2011). In the case of the MPP, a key objective is to speed up the entry of generic competition to bring down prices for newer patented anti-retroviral drugs and facilitate the development of new fixed-dose combinations and formulations adapted in resource-poor settings. The conditions of the licenses are negotiated between the licensor with MPP. The MMP also manages the pool of patents and licenses with third parties. All licenses are published in full.[38]

Another example of a voluntary initiative to facilitate licensing and opportunities for collaboration is the WIPO Re: Search, an open centralized database system run by the World Intellectual Property Organization (WIPO). Any party can offer IP, but also non-patented proprietary information such as know-how and services, to be included in the database. A number of pharmaceutical companies are currently members. For both providers and interested potential users, the system reduces transaction costs of seeking information and licenses. Under the WIPO Re: Search, parties commit to certain guiding principles the licenses are not centrally managed. This means that there is ample scope to negotiate the terms of the licenses, other than the broad terms prescribed by WIPO Re: Search, for instance the commitment of providers to grant royalty-free licenses for the use and sale of products under the license in all least developed countries. A summary of collaboration agreements, but not IPR licenses and their terms are published.[39]

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[36] A third alternative is the use of non-voluntary measures. Governments can issue compulsory licenses and government use to allow production and sale of a patented-drug without the authorization than the patent holder. These can be issued on various grounds, such as when a patent holder refuses to grant a license on reasonable terms (refusal to deal) or for public interest for instance when prices of the drug are considered too high, or to remedy anti-competitive practices.

[37] A patent pool is a voluntary measure, whereby any patent holder can make available a patent to the pool for the purpose of facilitating licences.

[38] See http://www.medicinespatentpool.org/current-licences/

[39] See http://www.wipo.int/research/en/collaboration.html.

It has been noted that facilitating use of patented information and know-how for innovation in neglected diseases requires a change in mindset from the patent holders to be more open to managing their IPR flexibly (Hoen E. et al. 2011). Indeed, this appears to be the greatest obstacle given that the profit prospects for academic and industry PDP partners in the area of neglected diseases are low or inexistent. Banerji and Pecault describe the difficulties of a PDP in negotiating a licensing agreement with a university: "throughout the protracted negotiations, staff at the university's business development department were supportive of DNDi's IP policy and commercial goals. The main obstacle was simply the difficulty faced by the legal representatives when asked to step away from the standard pro forma protocol and negotiate an agreement that flew in the face of their obligation to negotiate the best return on IP." (Banerji and Pecault 2007).

PDPs as "producers" of IPRs

PDPs may choose between the various alternatives for the appropriation of results derived from R&D projects through IPRs: the PDP does not seek IPRs; neither the PDP nor partners seek IPRs; the PDP and partners jointly seek IPRs; PDP seek IPRs; or partner seeks IPRs. It is expected that these choices may vary among PDPs and even across R&D projects of a PDP on a case by case basis, in accordance to a variety of factors, such as whether the PDP has a pre-defined IP policy, the specific disease (i.e. if there is any commercial market potential), the target profile of the product to be developed, the stage of R&D and the type of partner(s) involved. PDPs are generally involved in R&D for diseases that have no or little commercial market potential, though there is significant variance among diseases. Table 3 illustrates the diseases that PDPs are working on and their market characteristic.

The term "producers" of IP is used in this study to refer to ownership of IPRs by PDPs. The exclusionary effect of IPRs and potential impact on monopoly pricing and restriction of competition appears at odds with the mission of PDPs that is to make innovations accessible to all based on health needs. Patents are one of various factors that may affect prices and affordability of medical products, as it confers the patent holder monopoly rights over the marketing of the product for the period of the patent protection. Medical products in general, where available, are largely unaffordable for large populations in developing countries. Thus, the protection of IPRs by PDPs may cause tension with their global access mission. Moreover, it is well acknowledged that patents are not an effective mechanism to stimulate R&D in neglected diseases given that opportunities to make profits do not exist to begin with (World Health Organization 2006). This is more so the case

for not-for-profit innovation where the profit - motive is inexistent.

Table 3. Disease coverage by PDP[40]

	Product Development Partnership	Disease covered	Parallel Commercial market
1	Malaria Vaccine Initiative (MVI)	Malaria	Yes
2	Consortium for Parasitic Drug Development (CPDD)	African trypanosomiasis, leishmaniasis	No
3	Dengue Vaccine Initiative (DVI)	Dengue	No
4	European Vaccine Initiative (EVI)	Malaria, tuberculosis, HIV, Chagas, dengue, leishmaniasis,	Yes No
5	HIV Vaccine Trials Network (HVTN)	HIV	Yes
6	IVCC	Vector control	Yes
7	Meningitis Vaccines Project (MVP)	Meningitis B	No
8	Sabin Vaccine Institute PDP	Soil-transmitted helminths, schistosomiasis,	
9	South African AIDS Vaccine Initiative (SAAVI)	HIV	Yes
10	Tuberculosis Vaccine Initiative (TBVI)	Tuberculosis	Yes
11	Microbiocides Development Programme (MDP)	HIV	Yes
12	Foundation for Innovative New Diagnostics (FIND)	Tuberculosis, malaria, african trypanosomiasis, chagas	Yes No
13	CONRAD	HIV	Yes
14	Drugs for Neglected Diseases Initiative (DNDi)	Malaria, HIV, african trypanosomiasis, leishmaniasis, chagas, filarial diseases	Yes No
15	International Vaccine Institute (IVI)	cholera, typhoid	Yes
16	International Partnership for Microbiocides (IPM)	HIV	Yes
17	Global Alliance for TB Drug Development (TB Alliance)	Tuberculosis	Yes
18	Medicines for Malaria Venture (MMV)	Malaria	Yes
19	Institute for One World Health (iOWH)	Malaria, soil-transmitted helminths, leishmaniasis,	Yes No
20	The International AIDS Vaccine Initiative	HIV	Yes
21	IDRI	Malaria, tuberculosis, leishmaniasis, chagas	Yes No
22	AERAS	Tuberculosis	Yes

Accordingly, the model of knowledge management that one could expect to be preferred by not-for-profit innovative ventures would be one of no IPRs at all, particularly patents. That is, it is expected that PDPs would be "passive" rather than "active" producers of IPRs. As noted in Maurer et

[40] The diseases listed are all "neglected" in that they mainly affect developing countries, particularly poor settings and there is a dearth of R&D on new medical products with respect to the social need. This table draws a distinction between neglected diseases that in the absence of any policy (economic or regulatory) incentives nonetheless draw variant levels of commercial interest (i.e. market in developed countries) from neglected diseases which draw none at all.

al. 2004, there are significant benefits of an open source discovery model for neglected diseases in sharing capabilities and containing costs, while private firm collaboration can be incentivized via contract payments as an alternative to IPRs (Maurer et al. 2004). Moreover, the PDP model has the advantage that payment for the cost of R&D is delinked from the prices of medical products.[41]

That said, some PDPs reveal that they may file patent applications and use other forms of IPRs as part of their business model – as "active" producers of patents. A patent right allows the PDP to decide who can use the patented product and set conditions for use. Table 4 explores the possible intended functions of patents for PDPs and analyses the likelihood of these being pursued by PDPs.

Table 4. Functions for why a PDP may patent

Function	Likelihood
A. Incentive for monopoly pricing	No. Not consistent with the not-for-profit mission to provide access.
B. Revenues for financing activities	No. Not consistent with the funder funding model if financing is assured. PDP financing of R&D is de-linked from product sales.
C. Enhance powers of transaction	Yes. For instance, a PDP may condition licenses to produce specific amounts of product to be sold at low price, or negotiate terms of use/license to third party patents in return for use/license to the patents held by the PDP (cross-license).
D. Prevent private appropriation by third parties	Yes. For instance, to control use of the product and avoid monopoly pricing by third parties if these filed patents.
E. Raise interest of partners in manufacturing and distribution.	Yes, in particular for large, for – profit pharmaceutical firms.
F. Managing different worlds	Yes, for diseases commanding a dual market. For instance, patents may be licensed for use in developed countries in return for royalty payments to the PDP, while assuring low product prices in developing and least developed countries.

[41] PDPs seek financing for R&D from external sources; donations and grants by public and philanthropic institutions allow PDPs to maintain a not-for-profit status. Donors, in support of the public health objective of PDPs, could require PDPs to openly disclose and disseminate R&D results to facilitate follow on research, and oversee that these results are not privately appropriated or that IPRs are enforced in ways that restrict further innovation and access to medical products. However, there is no public information to suggest that donors systematically define rules concerning IP management as conditions for overall funding or grant disbursements to PDPs.

Given the broad number and diversity of partners and R&D projects of PDPs, it is assumed that decisions by a PDP on whether to file a patent are either defined by an pre-established IP policy as a baseline (with some degree of flexibility) or are taken on a case-to-case basis.

Interaction user and producer PDP

It is assumed that there is, in specific cases, an interaction between the role of a PDP as a user of IPRs and the role of a PDP as a producer of IPRs. For instance, to improve negotiation capacity to use third party patents, a PDP may seek patents from its R&D portfolio as a bargaining tool for cross - licensing. Likewise, a PDP that is a passive user of patents -in the case of PDPs that mainly disburse funds and outsource R&D to partners- is likely to also be a passive producer of patents. In contrast, a PDP that is at the forefront of the technology may be a passive user of patents but either a passive or active producer of patents –subject to the choice of the PDP.

Whether a PDP is an active producer of patents may also be related to the extent to which the PDP allows third parties to pursue patents or not. It has been noted that PDPs have a high degree of autonomy and freedom in their work to make alliances and strike deals, through licensing or contracts, to pursue their objectives (World Health Organization 2006). In situations where a PDP is able to cover the costs of the activity of the partners in the R&D project (presuming they engage on a voluntary basis in agreement with the common public health objective), it would not appear that partners would need additional incentives in the form of IPRs would be necessary or desirable to engage partners in R&D collaboration. However, variance can be expected in the terms of the deals that PDPs strike with partners. Variance may be dependent on numerous factors including the disease area (whether there is commercial potential in a segment of the market or application of the technology in other diseases with attractive markets), the bargaining position –power balance- of the PDP *vis a vis* the partner in the particular negotiation related to the "value" of the technology, the experience of PDPs in IP related negotiations, and the inclination of the PDP to adopt business-like practices with respect to IPRs. As an example, a PDP may allow an industry partner to reserve the right to claim patents for the innovations derived from the results of the PDP-led R&D project for the same indication in markets of commercial interest to the partner, (i.e. in the case of HIV/AIDS or Malaria in developed countries) known as "dual market or market segmentation", or for other indications. Likewise, PDPs may request that partners make access commitments to ensure affordability of the product once developed, such as not claiming IPRs for the application of the R&D project.

Limited information is available concerning these practices to allow for a detailed examination. Nonetheless, it provides a backdrop for the analysis of the question that concerns this study in assessing how PDPs manage IP related questions, in accessing technology or know-how for their R&D projects, in engaging partners into R&D projects, or in making use of IPRs on their own or with partners to pursue their public interest objective.

3.4 Method

This study is based on a survey of PDPs and an analysis of patents granted to PDPs. The study aimed to cover the whole population of PDPs.[42]

3.4.1 The survey

The initial sample was list of 23 PDPs. The survey questionnaire was built from in January 2014 and integrated into an on-line platform to allow for the response to be done remotely. The final sample was a list of 22 PDPs.[43] The total response rate for each survey completed was 76%.[44] The target respondents for the survey were the individual(s) responsible for IP within the PDP. We communicated with the PDPs to allow self-identification of the appropriate survey respondent. Most of the respondents were legal counsels.

The survey was composed of multiple selection questions and open response questions. The multiple selection questions also allowed the respondent to add comments. The questions concerned the importance of IP management for the PDP, the benefits or limitations of having IP poli-

[42] These PDPs were selected in accordance to the definition in Section III.1, developed in Munoz et al 2014.

[43] The initial sample included Pediatric Dengue Vaccine Initiative (PDVI) and Dengue Vaccine Initiative (DVI). PDVI finalized its work and continued as DVI. The sample includes Institute for One World Health (iOWH) as an independent entity though it has now merged with PATH and is now named "medical product development program". The sample also includes Consortium for Parasitic Drug Development (CPDD) and Microbiocides Development Programme (MDP), that are no longer in operation.

[44] The 16 PDPs that responded the survey were Drugs for Neglected Diseases Initiative (DNDi), Tuberculosis Vaccine Initiative (TBVI), Dengue Vaccine Initiative (DVI), Global Alliance for TB Drug Development (TB Alliance), IVCC, International Vaccine Institute (IVI), Malaria Vaccine Institute (MVI), Foundation for Innovative New Diagnostics (FIND), Sabin Vaccine Institute PDP, International Partnership for Microbiocides (IPM), Medicines for Malaria Venture (MMV), Meningitis Vaccines Project (MVP) of PATH, AERAS, CONRAD, European Vaccine Initiative (EVI) and Microbiocides Development Programme (MDP).

cies, factors that influence the PDP approach to IP management, internal governance structure for IP management, activities in relation to IP management, the use of third-party IPRs by PDPs, the types of IPRs that PDPs produce and their motivations for doing so, the extent to which PDPs consider collaboration to be useful, policy on claiming results from collaborative R&D projects, factors that influence patent licensing agreements or R&D agreements, the extent to which patents held by the PDP or by partners can be obstacles for successful conclusion of partnership agreements, whether PDPs have had cases of patent litigation or infringement.

3.4.2 Patent data

A search was undertaken for patent applications and granted patents for the 23 PDPs identified, using Thompson Reuters and Spacenet. The search was conducted for the period 1990 – 2014, for all national patent offices covered. Patent families are counted as a single patent. There are some differences in method amonsgt the two systems. In Spacenet, patent documents that all have the same priority number and appear as "also published as" documents. While Spacenet harmonizes equivalent documents, Thompson finds individual patent documents (raw data).

3.5 Results

3.5.1 Survey Results

This section summarizes the survey results. The full survey is available in Table 11 the appendix.

Importance of IP management and policy

The majority (67%) of PDPs indicated that IP management is important for the PDP. No PDP considered IP management to be of low importance.

Most PDPs report having a defined IP management policy (87%), however most PDPs do not make the IP management policy publicly available (62%). Most PDPs consider that a defined IP management policy has the benefit of providing clarity internally (management team, board) and exter-

nally (donors, partners) and as guidelines for decision-making, negotiations and to execute agreements with third parties (i.e. contracts, material transfer agreements, sublicenses, business plans). The IP policy set the scope of what is permitted or not, and how the PDP operates on IP matters. Other benefits of IP management policies that were noted included consistency and speed in decision-making and standardization between partners. It was also noted that an IP policy ensures that programs can be advanced without any potential or perceived barriers. Similarly, it was noted that an IP policy serves to ensure that products will be made available to the target populations in low income setting at affordable prices. One PDP noted that the IP policy serves to assure its private sector partners that it is aware of the IP situation and will respect and promote IP protection for the benefit of the companies and for the benefit of the public sector.

One PDP was of the view that not having a defined IP management policy is beneficial because it adds flexibility.

Characteristics of the PDP that influence the PDP approach to IP management

The characteristics of the PDP that influence the PDP approach to IP management are the R&D plus access mission (88%), non-profit nature (81%), and that they work to large extent through R&D partnerships/collaborations (75%). Another characteristic noted is that PDPs advance products that have no commercial return.

IP management governance

Some PDPs have staff explicitly dedicated to IP management (44%) while many do not (56%). Diverse responses were received on the question on the internal governance structure for IP management. In some PDPs, the responsibility lies with the head of legal (i.e. director or counsel). One PDP uses a consulting firm. In some PDPs the responsibility is shared or lies with business development, or with the head of R&D portfolio management. In some PDPs, IP decisions require approval of executive management (i.e. Director General). In some PDPs, IP decisions are brought to review bodies, such as an executive board committee or a portfolio management committee, a programme liaison group or programme management board. In some PDPs there are no committees or review bodies with such functions. One PDP noted IP management is a contract management function and it also responds to “clear donor guidelines.”

IP management activities

The survey asked PDPs to identify the main IP management activities it carries out. The responses varied. Some PDPs noted that IP issues are regulated in contracts and agreements with partners to serve various purposes. These included ensuring access provisions (that products will be made available at affordable prices) and freedom to operate (operate without infringing IPRs). Another purpose noted was the in - licensing of IPR-protected technology from third parties or to license from one party to another. Some PDPs report as main activity the filing of patents to protect inventions, including review of projects and publications and other disclosure for the timely filing of patent applications. The activities may also include protecting trade secrets and trademarks.

Other PDPs reported limited activities on IP management. Some PDPs report they do not hold any IPRs as a policy or practice, though they may include conditions on use of the technology in their agreements with partners or allow partners to claim IPRs under agreed conditions. It was also noted by a PDP that where partners are allowed to hold IPRs the PDPs does not support patent filing and prosecution costs. One PDP reported that its role is that of monitoring the IP situation, where all partners may hold IPR and have their own freedom to operate.

PDPs as users of IPRs

Most PDPs (75%) report they are a user of IPRs (described in the survey as "have gained rights or obtained a license to use third party IP-protected technology"). The main form of IPRs which PDPs seek use is patents (87%), followed by copyrights (40%) and trade secrets (40%), trademarks (33%). One PDP reported "data" as an additional input that PDPs use which may be protected by third-party IPRs.

The purposes of the use of patents vary. Those identified by the PDPs in the survey were to transfer technology to third parties (62%) to obtain access to a technology or knowledge that is protected by a patent (54%), for freedom to operate (54%).

The majority of PDPs consider of high importance (80%) to access the related know-how or capabilities of the patent holder, in addition to the right of use or license.

PDPs report that they never or rarely (76%) obtain an exclusive patent license (as opposed to non-exclusive). There is significant variance in the extent that PDPs may obtain royalty-free, as opposed to royalty-bearing patent licenses.

Some PDPs indicated that patent status of a technology does not influence the choice of that technology for an R&D project if it is considered the best technology for the project (47%). Other PDPs indicated that where there is alternative technology available to the patented technology, the PDP would choose alternative (27%).

Third party sharing IP with PDPs

The majority of PDPs (87%) indicate that it is useful for third parties to share patents (allow the PDP uncompensated use of a patent) with the PDP. Most PDPs noted that sharing is equally useful in all R&D stages (64%), while others noted that in early development/discovery it is more useful, or in process/product development. Two PDPs indicated that the royalty-free sharing of patents to the PDP would not be useful at all.

PDPs as producers of IPRs

Most PDPs reported to claim ownership of some form of IPR (69%). Others reported not to claim any IPRs (31%).

For PDPs that claim IPRs, the main form is patents (42%). Others include copyright, trade secret, trademarks and data. Some PDPs reported that technology and know-how is protected in agreements with partners. For instance, one PDP reported that it protects technology by requiring the partner to agree to transfer the technology if it is unwilling or unable to fulfil its obligations. Similarly, another PDP noted that it only reserves IPRs in case of a partners' non-compliance with contractual obligations.

There are several nuances in the patent strategies of PDPs. Some PDPs that do not seek ownership of patents nonetheless allow the partner to file patents. This may include allowing the patent holder to operate in the same area in which the PDP operated (in addition to allowing the partner to patent in relation to other areas of application of the invention, such as for other diseases with commercial markets). Conditions may nonetheless be placed by PDPs on the patent holder. One

PDP described that allowing a partner to claim patents is conditioned to a grant-back, royalty-free, non-exclusive license to the PDP to continue to use the patent in its activities.

The majority of PDPs have a policy on who may seek patents on the results of R&D projects (60%), while others do not (40%). The policies diverge significantly.

For PDPs that allow patents on results of the R&D projects, there are a variety of approaches. There is variance among PDPs on the decision-making process to define whether to file a patent (i.e. whether the PDP alone decides, the partner alone decides, or the partner and PDP decide together), who files the patent (i.e. the inventor or the institution) and what happens after the patent is filled (i.e. whether the patent is then assigned on).

Among the PDPs that claim patents a diverse of purposes were reported. One of the purposes reported is to license-on the patent to industry, raising their interest in partnering in manufacturing/distribution (50%). PDPs also reported that patents are used as part of a defensive strategy, to avoid third parties from unauthorized use of the technology or claiming ownership of patents over the technology (44%). Another strategic use of patents reported was to cross-license to access technology owned by third parties. Two PDPs reported to claim patents as a way to generate income via licensing to fund activities (13%). One PDP reported that a patent allows the PDP to exert control in the development and manufacturing of a product to ensure its proper use and quality. Another PDP reported it files patents to fulfil pre-existing obligations to commercial partners or funders.

With regards to the results of R&D projects in the PDP portfolio, a variety of IP approaches may follow. A partner can hold a patent, with pre-agreed licensing terms to the PDP (67%) or other conditions placed in the contract that the products must be made available at affordable prices in target populations. A PDP can hold a patent (60%). The PDP and partner or partners can jointly hold a patent (60%).

Sharing of IP by PDPs with third parties and open approaches to R&D collaboration

In the case of PDPs that claim patents, they are not generally allowing third parties to make uncompensated use of the patents. That said, some report doing so, or considering doing so, for cases where the use is for non-profit goals (i.e. with academic partners) or non-commercial uses by partners, or for a specific type of partner (academia). One PDP noted it is comfortable licensing

patents on an exclusive basis in developed countries and on a non-exclusive basis in least developed countries. Another PDP noted that it has cross-licensed or shared its patents in return for global access to the final product.

For most PDPs, open R&D collaboration (no patent claims for results of the R&D collaboration) is considered useful (67%), while others do not consider it to be useful (20%). Open collaboration was noted to be particularly useful in the discovery stage.

Patent and licensing agreements

A variety of factors were reported as influencing patent licensing agreements or R&D agreements between the PDP and partners. Some of the factors more often recognized were the R&D stage (80%), the target profile of the product to be developed (73%), the specific disease targeted (67%), the regions/countries targeted (60%), the type of partner (60%), the target price of the medical product (53%). Other factors noted were the choice of sources to obtain the technology/knowledge/resources (47%), the markets that are targeted (private, public, purchasing entities) (47%), the source of funds of the PDP (40%), the estimated cost of production (40%), and commitment to providing access to the product to those most in need in developing countries.

Patents as barriers

PDPs reported that pre-existing patents held by partners were sometimes (43%) or rarely (36%) an obstacle for the successful conclusion of partnerships at any R&D stage. In contrast, PDPs considered that the patents held by the PDP are never (79%) or rarely (21%) an obstacle for the successful conclusion of partnerships at any R&D stage. Negotiations on the terms for ownership of future patents were considered as sometimes (47%) or rarely (40%) an obstacle for the successful conclusion of partnerships at any R&D stage.

IPR infringement and enforcement

All PDPs reported that they have never sought opposition or invalidation of any IPR held by a third party. Most PDPs also reported that they have not had any cases of patent litigation or infringe-

ment to deal with (81% as compared to 19%). One PDP noted that it has been cautious to proceed with a particular compound that is held by a biotech company because of the patents surrounding that compound and the inability of the PP to obtain a license to that compound.

3.5.2 Patent data results

Table 5. Patents held by PDPs, operating model and disease

	Patents in Thompson - search all	*Patents in Spacenet*	*In-house R&D*
MVI	0	0	0
CPDD	0	0	0
DVI	0	0	0
EVI	0	0	0
HVTN	0	0	0
IVCC	0	0	0
MVP	0	0	0
Sabin	0	0	1
SAAVI	0	0	0
TVI	0	0	0
MDP	0	0	0
DNDI	2	2	0
CONRAD	1	1	1
FIND	0	0	0
IPM	4	4	0
IVI	3	3	1
TB alliance	25	5	0
MMV	96	15	0
IOWH	70	22	1
IAVI	89	36	0
IDRI	96	36	1
AERAS	67	65	1

The patent landscape results in Table 5 show high heterogeneity among PDPs in terms of their patent portfolio.

Over half of the PDPs (54.5%) do not hold any patents. Out of the PDPs that hold at least one patent (45.5%), half of the PDPs hold between 1 and 5 patents, while the other half hold between 15 and 65 patents.

All of the PDPs that work exclusively on diseases that have no potential parallel commercial mar-

kets have no patents. Three out of five PDPs (DNDI, iOWH, and IDRI) that work on both on diseases with potential parallel commercial markets and diseases with no commercial markets hold patents, between 2 (DNDi) and 36 (IDRI) patents. Of the thirteen PDPs that work on diseases with potential parallel commercial markets, six do not patent.

The three PDPs that have in-house R&D capacity hold patents; two of these PDPs are also among the PDPs that hold the most patents. A number of PDPs that focus on managing R&D collaborations and outsourcing the R&D activities also hold patents. These results are discussed in the next section.

3.6 Discussion

The survey results indicate that PDPs consider IP management to be an important activity. That said, there is a significant variance among PDPs in the approaches to IP management, as evidenced by the diversity of responses to the survey by PDPs and the divergence in patenting trends revealed by the patent data.

PDPs as users of IP

Most PDPs recognized the organization as a user of IPRs held by third parties, which indicate that the activities of PDPs involve some form of access to pre-existing background technology, know how or data. The purposes of using third party IPRs, as noted by over half of the surveyed PDPs, include either or all of the following: the transfer of technology to third parties; to obtain access to a technology or knowledge that is protected by a patent; and for freedom to operate. Approximately half of the PDPs responded that patent status of a technology does not influence the choice of that technology for an R&D project if it is considered the best technology for the project. This can be interpreted as an indication that PDPs are eager and able to gain access to patented technology by third parties, which may be the case because most PDPs are transferring to partners (or in the case of a few PDPs, developing themselves) technology that builds upon pre-existing technology (e.g. new drug formulations) as opposed to radical new innovations, and therefore there are limited alternatives to the patented technology. It may also be the case that such pre-

existing patents are not insurmountable barriers. One PDP noted that pre-existing patents is a minor issue on the broader decision of what R&D project to pursue.

A third of PDPs responded that where there is alternative technology available to the patented technology, the PDP would choose alternative. One explanation is that the PDP would rather avoid royalty payments due from licenses or otherwise the transaction costs of entering into negotiations with patent holders. This interpretation is also supported by the fact that the majority of PDPs indicated that it is useful for third parties to share patents (allow the PDP uncompensated use of a patent) with the PDP.

Two PDPs indicated that the royalty-free sharing of patents to the PDP would not be useful at all. It is interesting to try to interpret why a PDP would consider this to be the case, as an assumption in this study was that PDPs would aim to avoid the exclusionary effect of patents. For one of the two PDPs (TBVI), it appears that the PDP does not consider it would benefit from royalty-free access to a patent as the PDP does not seek to make use of the patented technology (the PDP indicated it does not does not use any IP and in principle no IP is owned by the IP). It would also appear that the PDP does not play a role in the transfer of technology to third parties. The second PDP (DVI) noted that the PDP mainly monitors the IP situation (although inventors can apply for a patent and assign it to the PDP) and does not consider that the field is impeded by competing or overlapping IP claims. This last assertion may be particular to the specific disease area where DVI operates –dengue- on which it has been reported that there is low degree of overlap among patents related to dengue vaccines under development (Krattiger et al. 2012). However, this may not be the case for other diseases as has been found in the case of Malaria, tuberculosis and HIV/AIDS[45].

Importantly, for the large majority of PDPs it is very important to access to the related know-how or capabilities of the patent holder, in addition to the right of use or license. As noted prior, most PDPs are involved in the transfer of technology to partners. Patents provide information but the replication of a patented-technology can be complex, largely due to the tacit elements of knowledge that make it difficult to transfer. Therefore, effective technology transfer by the PDP, measured by the ability of the partner to "learn" how to absorb and adapt the background technology, requires that the PDP can access and provide to the partner these additional inputs in addition to

[45] The UNITAID Medicines Patent Pool makes available data on the patent status of selected HIV medicines in low and middle income countries, see http://www.medicinespatentpool.org/patent-data/patent-status-of-arvs/.

the patent. Accordingly, IP clauses are usually part of broader R&D or technology transfer agreements, rather than single in-licensing or out-licensing deals.

PDPs as producers of IP

The survey and patent data results show divergence in the extent that PDPs are producers of IPRs. The initial assumption of this study was that PDPs would not be inclined to seek patents and prefer open collaborative model of R&D and innovation to avoid the exclusionary effects of IPRs. That said, it was also foreseen that a number of factors could influence the decision of a PDP to patent, as summarized in Table 2. In addition, two PDP characteristics were also considered alongside the patent data results in Table 3. The first being whether the PDP has in-house R&D capacity on top of a role in managing collaborative R&D and disbursing financing to third parties. The second was whether the diseases in which the PDP carries out R&D have or not parallel commercial markets. The patent data results showed that PDPs that work solely on diseases for which there is no potential parallel commercial markets do not patent. This is consistent with the initial assumption that PDPs would not be inclined to seek patents. However, the reverse case does not hold true. There is no trend in the patent data to indicate that PDP that work on diseases for which parallel markets do exist tend to seek patents. In contrast, whether a PDP has in-house R&D capacity does appear to be associated to an increased interest in seeking patents.

As in the case of the patent data, the results of the survey on PDPs as producers of IPRs also showed significant divergence among PDPs. Approximately half of the surveyed PDPs have no or very little activity in terms of filling applications, either as a practice or as a principle made explicit (publicly available) or implicit (not publicly available) policy of not filling any patents. This result is consistent with the earlier proposition in this study that PDPs, as not-for-profit entities that aim to ensure access to new medical products, would prefer open approaches to innovation as opposed to producing patents. The PDP can promote that knowledge remains in the public domain. The survey reveals that PDPs consider the decision on the basis of pursuing the mission and objectives of the PDP.

In some PDPs the decision whether to patent or not, or potentially to allow partners to patent, is a strategic one, while for others it reflects the low priority that IPRs represents for the PDPs. A limi-

tation in this analysis is that from the survey and patent data it is not possible to observe whether PDPs that are not patenting are nonetheless allowing partners to seek patents and under what conditions, if any. This would be important in understanding the strategic decision of a PDP not to patent versus allowing partners to patent (potentially as an incentive mechanism for the partner to enter into collaboration with the PDP). The survey reveals that some PDPs that allow partners to patent in respect to results of PDP-led R&D projects. However, the PDPs generally place conditions that are defined in contracts related to the access mission of PDPs (i.e. grant back license to the PDP for continued use in the specific field, making available products at affordable prices in developing countries, requiring technology transfer if the partner is unwilling or unable to fulfil its obligations).

The other half of the surveyed PDPs is a group of producers of patents. Each PDP in this group holds at least one patent and up to 65 patents. In effect, patents allows a PDP to exclude others from making, using, selling and importing the protected product, which raises concerns on the enclosure of knowledge, particularly when financed from public and philanthropic financing. We explored in the Table 1 in this study, various ideas where explored for why PDPs may pursue exclusionary patent rights. As expected, the survey results show that monopoly pricing by the PDP is not a motivating factor. Rather, PDPs may seek patents, in cases where the alternative would be to allow a partner to patent, in order to gain an upper hand in negotiating licensing terms. The survey results also show that PDP patents may be linked to raising the interest of for-profit pharmaceutical firm or other private sector partners in an R&D project, particularly at the stage of manufacturing and distribution, or to strengthen negotiation position for obtaining licenses to third-party protected material or know-how (cross-licensing). It can be a risky proposition, requiring able negotiation skills on the part of PDPs to obtain a licensing deal that strikes an adequate balance between access and affordability objectives while leveraging the commercial or other interest of the partner. It also requires a PDP to invest resources into obtaining, maintaining and enforcing patents. However, the alternative of the PDP allowing partners to patent material developed from PDP R&D projects, subject to negotiated conditions, may be a simpler, but high risk formula. It requires that PDPs have strong negotiation capacity and means for enforcement in cases of non-compliance of the contractual conditions. The outcomes of licensing deals, from patents held by PDPs or partners, are not observable from the survey. The alternative of neither the PDP nor partners seeking patents would have the benefit of allowing the knowledge to be in the public domain, which facilitates follow-on innovation and the pace at which the products can reach those in need. The main obstacle is ensuring financing for manufacturing, scale-up and distribution.

The survey reveals that external factors, such as regulations or prior contractual commitments, can affect the PDP decision to patent. For example, one PDP noted that it is required by the funding agency to seek patents and engage in licensing on the terms pre-defined by the funding agency.

Contrary to the expected results, two PDPs reported a motivation to produce IPRs to earn revenues to invest in their activities.[46] The result appears to be at odds with the financing model of PDPs. However, it may be a strategy consistent with the PDP mission in cases for diseases with dual markets. In such cases, PDPs can earn licensing revenues from developed countries where there are buyers for the PDP licenses willing to pay a higher price for the patented technology, while maintaining low prices for developing and least developed countries. Some other unexpected responses by PDPs were that patents are sought to enable the PDP to "control the development, manufacturing of a compound to ensure proper use, quality and access" and to "ensure access to products at affordable prices in the target populations". The responses appear to indicate a sense of risk in allowing third parties either to patent the material or to make inadequate use the material. That said, there is no direct link between patent protection and the quality or proper use or affordability of a protected product. All medical products require regulatory approval before they can legally be sold on the market. It is a qualitative judgment on the role of PDPs but not a basis for defining whether an exclusionary patent right is warranted. With respect to pricing, in a situation where there are no patents held by any party, increased competition from additional producers of the products would aid to drive prices down. The main problem in the area of neglected diseases is that there is insufficient interest in the first place in R&D for new medical products.

Sharing of IP and open approaches to R&D collaboration

Contrary to the assumption of the study of PDPs of being favourable to open innovation due to their not-for-profit mission and public and philanthropic financing, the evidence is limited. While PDPs report being open to R&D collaboration (no patent claims for results of the R&D collaboration), and find useful for third parties to share patents, they are not generally allowing uncom-

[46] The Infectious Disease Research Institute (IDRI) is an example of a PDP with a policy to license patented technologies it develops to third parties (i.e. biotechnology companies) for applications outside of the scope of neglected diseases (i.e. cancer) to reinvest royalties from licenses in its activities (Global Health Technologies Coalition 2013).

pensated use of the patents by third parties or only for very specific cases. It is not possible to observe from the survey results whether there is distinction between diseases that command dual markets and those that do not (arguably where commercial markets exist the PDP may seek royalty payments for use of the patent).

Patent and licensing agreements

As expected, the terms of patent licenses and R&D agreements that PDPs negotiate and obtain can vary on a case-to-case basis, influenced by a number of factors. These include the target profile of the product to be developed, the R&D stage, the disease, the regions/countries targeted and the type of partner. This results in a wide diversity of outcomes, which are not readily observable as the terms of patent license deals and R&D agreements are for the most part confidential.

Patents as barriers

The survey shows that patents held by third parties can be an obstacle for the successful conclusion of partnerships at any R&D stage, while patents held by the PDPs are seen as less of an obstacle. One PDP noted that it has been cautious to proceed with a particular compound that is held by a biotech company because of the patents surrounding that compound and the inability of the PDP to obtain a license to that compound. Disagreement on the terms for ownership of future patents can also be an obstacle in negotiations among PDPs and partners.

IPR infringement and enforcement

As noted previously, the threat of litigation in relation to a pre-existing patent can deter a PDP from pursuing a technology. That said, patent litigation due to patent infringement is not a regular practice for PDPs, though PDP partners may be involved in patent litigation. There can be various interpretations for this finding. For instance, it may be that obtaining licenses to the PDP patented technology is not difficult, or there may be few players involved in R&D in the same area, or that the patents are not strictly enforced by PDPs.

3.7 Conclusions

Inventions in the area of public health can be developed as public goods to ensure dissemination and access to all populations. Models of innovation that de-link the costs of R&D and innovation from the prices of medical products, such as that employed by PDPs in the area of neglected diseases, can serve this purpose. PDPs are an institutional experiment that aims to respond to dearth of private R&D for neglected diseases, that present no or very small commercial markets. PDPs have demonstrated that it is possible to bring about innovation in medical products as public goods.

Given the above, an early assumption of this study was that patents and other IPRs would play a very limited role in the framework of PDPs not-for-profit innovation. The findings show that consistent with other literature, IPRs do not act as an incentive for R&D and innovation in PDP institutions in the same sense as IPRs are expected to do so for private, profit-maximizing firms. However, the management of IP more broadly is an activity of relative importance for PDPs, as potential "users" of background IPRs held by third parties over technology, data or know-how that the PDP seeks to access, and as "producers" of IPRs. Accordingly, this study finds that PDPs use IP for strategic purposes to advance their not-for-profit and access mandate. This requires significant skills from PDPs to manage the "IP labyrinth" in aiming to ensure that IPRs do not become barriers to access to medical products and further innovation, particularly in cases where PDPs allow partners to patent or grant partners exclusive licenses to a PDP-held patent.

PDPs are playing an important role in advancing R&D in areas where there is under-investment from the private sector. Nevertheless, PDPs remain institutional experiments whereby long-term sustainability is not ensured. Policy makers are encouraged to pay closer attention to the evidence of the strategic use of IPRs by PDPs as not-for-profits that are funded through public moneys and manage R&D collaborations involving private firms. The public health community can increase oversight of PDP activities and request greater transparency to ensure that PDPs and their partners manage IP in a manner that does not hinder access. A limitation of this study is that the impact of IPRs held on the results of PDP R&D portfolios, whether held by PDPs or by partners, was not observed. The study was also unable to observe the conditions of the IPR licensing, contracts, technology transfer, R&D and other agreements between PDPs and R&D partners or other third parties (i.e. donors), which may also define conditions on use of IPRs.

Finally, a broader lesson for the economic analysis of patenting activities can be derived from this study. Beyond the basic feature (IPR holder can exclude others from use), IPRs can serve very different interests and functions according to the institutional nature of the patent holder. The economic analysis of IPRs tends to study the social and economic effects of IPRs disconnected from the analysis of the institution that produces and manages them. However, as this study shows, there is much that can be learned about the effects of IPRs by linking the analysis of the use of IPRs with the analysis of the nature of the institution producing it. For example, this study finds important particularities in the IP management by a private agent beyond the for-profit firm (the usual unit of analysis in economic research on IPRs). Accordingly, the economic analysis of IPRs should do more studies on the functions of IPRs and IP management activities in connection with the institutional nature of the IPR holder.

Chapter 4 The Role of Institutions in Support of Traditional Medical Knowledge[47]

Experiential knowledge is a valuable form of knowledge. By nature, it is fragile and more likely to suffer from deterioration or even disappearance, as compared to scientific knowledge. The loss of experiential knowledge leads to reduced capacity for effective action in certain socioeconomic contexts and circumstances in which such knowledge was previously useful or can be useful. In this study we examine in particular the case of traditional medicinal knowledge. We advance that in light of the deterioration of traditional institutions, the formation of supportive new institutions can assist to at the least attenuate the rate of loss of useful traditional medical knowledge, and promote its use and reproduction to address local health needs and for the advancement of modern medicine.

4.1 Introduction

Knowledge empowers human beings with the ability to act on a physical or intellectual level. This ability to act is exercised in the domains of production, consumption, and also anticipation. Knowledge is thus "expertise" or "competence" that is embodied in people, and can range from general to specialized.

The study of economics of knowledge has emphasized the role of scientific codified knowledge production and diffusion in the context of knowledge-based economies (Foray 2006). Scientific, formal knowledge is important to develop capabilities for technical, knowledge-intensive innovation and tapping into global knowledge. However, different kinds of knowledge and knowledge systems are also relevant to meet the needs of today's world. The dynamics of experiential knowl-

[47] This Chapter is based on a paper developed in collaboration with Dominique Foray.

edge is one area that is understudied, despite its important role in many fields such as environmental conservation and research (Fazey et al. 2006).

Knowledge is often *experiential* in nature. That is, it springs form the experience –active involvement- of individuals and organisations. Experiential knowledge is not anti-scientific; it has simply not undergone the tests that give a piece of knowledge the scientific status. It is nonetheless wide-ranging, sound, rational and effective in a particular circumstance or life event. No doubt it is less general than other knowledge since the experiences that generated it are local and specific. Experiential knowledge is a valuable source of prior knowledge. We know from educational research that ones' prior knowledge or existing knowledge base is pivotal for subsequent learning. Moreover, while experimental knowledge is rooted in past experience, it is a source of knowledge to be utilized in future action.

Experiential knowledge can be *private* or *collective* in nature. *Private* experiential knowledge includes know-how, manual skills, practices that are kept secret or shared by a small number of individuals. *Collective* experiential knowledge is held and exercised by a community, tribe or population, such as know-how and techniques used in daily life.

A specific form of experiential knowledge is *traditional* knowledge that has been build up over time and is held locally, and informs shared understandings, beliefs, practices, social interactions, etc. It is a source of valuable experiential knowledge such as on uses of natural resources that are most relevant in connection to sustaining local livelihoods and sustainable development. *Traditional medicinal* knowledge plays an important role in public health, particularly in countries where it is the main or sole source of health care. It also has modern applications in fields such as pharmaceuticals and biotechnology that in turn has increased the interest in its use beyond the local context, as evidenced by the number of government policies aiming to generate economic value from its use (World Health Organization 2013).

The central argument of this study is that in the absence of traditional institutions that served to support traditional medical knowledge reproduction and transmission, such knowledge becomes fragile and is more likely to suffer from deterioration or even disappearance, as compared to scientific knowledge. The loss of traditional medical knowledge leads to reduced capacity for effective action in certain socioeconomic contexts and circumstances in which such knowledge was previously useful. We advance that more efforts should be directed at building institutions to sup-

port the reproduction and transmission of traditional medical knowledge to meet health needs at the local level, as well as national and global level.

Following this introduction, Section 2 explains the main elements of the economics of knowledge, as a basis to analyse the fundamental problems raised by the nature of experiential knowledge, emphasizing the general difficulties in its reproduction and transmission due to its tacit and local character. Section 3 describes traditional medical knowledge, as compared to other forms of medical knowledge, the role of traditional institutions in the local community context, and discusses market failures in relation to broader applications of traditional medical knowledge. Section 5 discusses the critical role of institutions in supporting traditional medical knowledge. Section 6 focuses on the institutions of intellectual property and access and benefit sharing laws. Section 7 concludes.

4.2 The economics of scientific and experiential knowledge

Looking at and comparing between the organisation of scientific knowledge production and distribution, and the disorganisation of experiential knowledge, one can easily contrast the current strength and vigour of the processes of creating, codifying and circulating scientific know-how and the fragile nature of experiential knowledge. This contrast is characteristic of numerous domains: health, environment, food security, regional planning and development, natural risk management.

In comparing the strength and vigour of the creation and management processes of scientific knowledge with the fragility of experiential knowledge, we must ask ourselves to what extent the difficulties of a market system to correctly allocate resources in the knowledge production and management domain are more serious or less well corrected in the area of experiential knowledge than in that of scientific knowledge.

This question was not relevant during “the good old days” when traditional institutions and norms were rather effective in supporting the creation, improvement and distribution of experiential knowledge such as in the case of the traditional medical knowledge (to which we will turn below). However, as this system of institutions becomes less robust and is collapsing, then the question of what socio-economic institutions can be relied upon to produce and distribute experiential knowledge in an efficient manner becomes central.

We will first discuss the set of institutions that play this role in the case of scientific knowledge and then ask whether such institutions could be extended to the case of experiential knowledge, as a substitute of the traditional institutional framework that is slowly disappearing.

4.2.1 Market failures and institutional solutions in the case of scientific knowledge

Economists tend to identify three generic causes of market failure (see for example, Swann, 2003). The first is that externalities drive a wedge between private and social returns from a particular private investment. If externalities are positive some socially desirable investments will not appear privately profitable, so the market does not support enough activity. If externalities are negative, then the private investments create a greater cost to society that to the consumer, as in the case of activities causing environmental degradation. The second is that economic activities are subject to increasing returns. The third is that of asymmetric information. The usual working hypothesis is that the most important source of market failure that arises in the context of the production and management of knowledge is the existence of positive externalities from such activities, such as research and development, whereby third parties are able to benefit without sharing the cost.

We can go further by distinguishing different types of externality that may give rise to these market failures.

**Public good externalities (Samuelson, 1954)*: a public good can be viewed as an extreme form of externality. It is defined according to two properties. First, it is difficult to exclude anyone from the benefits of a public good. Second, the marginal cost of enjoying the good is zero (consumption is non - rivalrous). Knowledge has both of these properties (it is difficult to exclude others from the benefits of the knowledge, and the marginal cost of an additional person making use of an idea is zero) and as with all public goods, private markets are likely to provide an undersupply of knowledge.[48]

**Ownership externalities (Bator, 1958)*: it is often difficult to attribute to a resource its real social value (the shadow value), which generates an inability to allocate resources correctly. This there-

[48] A whole series of phenomena exists that mitigate the public good nature of knowledge while not altering the economic logic of the argument. In particular, although it is correct to recognize that developing human capability to make use of knowledge involves processes that entail fixed costs, the existence of the latter does not vitiate the proposition that reuse of the knowledge will neither deplete it nor impose significant further marginal costs.

fore concerns the difficulty of measuring the social value of a resource and thus attributing to it a series of results to which its contribution is difficult to observe. Certain « goods » with determinate positive shadow values are simply not attributed, simply because « keeping account » on who produces and who gets what may be impossible, clumsy or costly in terms of resources. Clearly, this is the case of knowledge. Evidence about the positive (direct and indirect) effects of the production of knowledge in the society and the economy is difficult to build and it is also difficult to try to measure returns on individual research projects.

The difference between these two types of externalities is that in the latter case, the difficulty only concerns keeping account and might be eliminated if correct measurements are made and attribution devices set up. This is just a failure by enforcement (Bator, 1958). Whereas the difficulty revealed in the case of the first externality (public good) cannot be eliminated - this is a failure by existence (ibid). The public good nature of the resource implies that the price that would encourage private agents to produce the optimal quantity of this good would inevitably be inefficient as regards the allocation of this resource: because the marginal cost of an additional person making use of the knowledge is zero, the maximisation of allocative efficiency requiring prices equal to marginal cost will make the activity unprofitable.

**Tyranny of small decisions (Kahn, 1966)*: Finally a last type of externality seems important in the case of knowledge production and management. It expresses the fact that the market economy makes its major allocation decision on the basis of a host of 'smaller decisions' (smaller in size and time dimension). The tyranny of small decisions suggests that the total effect of small decisions may not be optimal, because the decisive determinations are individually too small – in terms of size, scope and time perspective. If one hundred consumers choose option x, and this causes the market to make decision X (where X = 100 x), it is not necessarily true that those same consumers would have voted for X if that large decision had ever been presented for their explicit consideration. According to Weisbrod (1964), there is an externality and hence a market failure when: a) the option is not (always) exercised; b) revenues from actual purchasers are insufficient to cover the costs of continued operation; and c) expansion or restarting of production at the time when occasional purchasers wish to make a purchase is difficult or impossible. The external benefit here is the mere availability of the service (or the knowledge) to non-users, the continued ability to satisfy as yet un-exerted option demand. The deterioration or even disappearance of a great deal of knowledge is often caused by this externality.

These different types of externality apply to both the scientific knowledge and experiential knowledge domains. However, science has developed institutions allowing them to be corrected or their effects to be attenuated and it would therefore be the presence of these institutions in one case and their absence in the other that could explain the contrast between the vigour and power of the creation and circulation processes of scientific knowledge and the fragility of experiential knowledge. An additional step is thus necessary to explain this contrast. This consists of identifying and assessing the institutional solutions that science benefits from but that are not applied in the other case.

Firstly, the institutional solutions allowing the problem of public good externalities to be attenuated are well known. Pigou was the first to identify the three mechanisms for providing public goods: directed governmental production, subsidies and regulated monopoly. These three mechanisms have a clear application in the domain of scientific knowledge production and R&D. The first mechanism consists of the government engaging itself directly in the production of knowledge; the second mechanism is one where production is undertaken by private agents who in turn are subsidized for their effort by the public purse. The third mechanism is to establish a competitive market mechanism for some type of knowledge to which private ownership can be legally assigned and whose ownership can be enforced (Dasgupta, 1988, David, 1993).

Secondly, the scientific institution has given rise to the development of institutional mechanisms to evaluate and even measure the intrinsic value of new scientific knowledge. According to the historical analysis of Paul David (2007), the competition for the “best” scientists between potential patrons required open science as a solution to the asymmetric information problem that the patrons faced, namely to identify the truly leading scientists of their generation. Only within communities in which full disclosure was exercised could the scientific findings be evaluated and discussed and credible reputations be established that would allow wealthy patrons to identify truly distinguished scientists from fraudulent ones. From these historical origins the institutionalisation of effective mechanisms for the systematic evaluation of scientific knowledge took place as a valuable solution to the Bator ownership externalities.

Finally, as in the case of many other types of public good, decisions regarding the allocation of resources to scientific research are delegated to administrative entities operating at the appropriate levels – usually at the national level but also in certain domains at the supra-national (case of the CERN) level, which allows the « tyranny of small decisions » effects to be avoided. Developing and protecting appropriate upper levels of decision-makers in science means that the fundamental

allocation choices do not occur by surprise *ex post* – as the result of a series of individual micro-decisions – but are made *ex ante*. Table 6 summarizes the types of externalities that can cause market failure in the production of scientific knowledge and institutions developed to correct them.

Table 6. Market failure in the production of scientific knowledge: externalities and institutional solutions

Type of externalities	*Examples of institutions to address externalities*
Public good	Subsidies, directed government production, regulated monopoly (intellectual property right)
Ownership	Open science as a mechanism for public demonstration and evaluation of the new knowledge
Tyranny of small decisions	Upper levels of decision making

And yet none of these mechanisms seems to really exist in the experiential knowledge domain. Or rather, you have to search thoroughly for a long time to discover more or less hidden mechanisms, likely to offer solutions to the problems of externalities - and that is the objective of the rest of the study.

4.2.2 How did experiential knowledge become fragile and is it an important socio-economic problem?

Traditional institutional arrangements (such as oral intergenerational passing on, role of traditional healers, community management of natural resources, customary law) worked generally well to address failures in knowledge management, in a broad sense, within their local context where the traditional and experiential knowledge was originally used (see for instance Goody,1998; Delbos and Jorion,2009; Perriault, 1993; Epstein, 1998).

But when traditional institutions come under strain (because of migration that dislocates communities, younger generations are no longer interested acquiring the knowledge passed down from other generations or are more interested in learning modern medicine, loss of social capital -trust among community members-, commercial interests become more prominent, loss of access to

local natural resources due to expropriation of land, competition with modern methods), traditional knowledge becomes fragile and new mechanisms are necessary to ensure its preservation and use.

It is a dangerous illusion to believe that a society could function solely on the basis of scientific knowledge - the sort of society that would have all the possible « vaccines » at its disposal to rectify problems and could therefore do without the experiential knowledge that is generally speaking applied beforehand to prevent these problems from ever occurring. The objective of the economics of knowledge is thus certainly not a society in which all the vaccines would be available, but a society in which the balance of the allocation of resources between scientific knowledge and experiential knowledge is properly protected.

If experiential knowledge and scientific knowledge are not substitutable, as it is claimed above, then the disinvention problem (loss of knowledge) may be socially costly if the experiential knowledge considered was valuable in certain contexts and circumstances and these circumstances are likely to happen again. It is therefore useful to identify some potential solutions and institutions that can be relied upon to maintain, reproduce and exploit experiential knowledge; that is institutions that can sustain an efficient “infrastructure” to reproduce this particular type of knowledge.

4.3 The important but insufficient role of codification

In view of these problems, the museum solution rapidly springs to mind. Societies have built and sustained institutions – such as libraries, archives and museums – to collect, organize and provide access to knowledge-bearing objects for more than two millennia (Hedstrom and King, 2006). It is, therefore, legitimate to think of a potential role for this so-called “epistemic infrastructure” when issues of knowledge loss and of disinvention need to be addressed. This calls to mind the UNESCO project aimed at setting up a world bank in Florence to make an inventory of, safeguard and promote traditional know-how.[49] This is certainly a laudable objective. However, as already stated, experiential knowledge involves more than a mere catalogue of traditional techniques. Museums are no doubt necessary but under no circumstances sufficient to obtain the appropriate balance between scientific know-how and experiential knowledge. The main question is therefore less that

[49] See www.tkwb.org

of the creation of libraries or conservatories than that of the capacity of living communities to adapt and utilise their experiential knowledge within the framework of their current socioeconomic activities; in other words, to attribute a certain economic value to this knowledge.

Certainly the codification of experiential knowledge is an important tool. Knowledge codification involves a set of operations aiming at detaching the knowledge from the person in possession of it, with a view of inscribing it in a medium. The process starts with some forms of modelling of tacit knowledge (ranging from delivering a simple but careful description to building complex systems of causal relationships) and may require the mobilization of languages other than natural language (Foray, 2006). Through a codification process, a piece of knowledge is detached from the individual and the memory and communication capacity created is made independent of human beings. Although it involves high fixed costs, codification also enables agents to perform a number of operations at a very low marginal cost (Cowan et al. 2000). It reduces the costs and improves the reliability of storage and memorization. As long as the medium remains legible and the code has not been forgotten, codified scripts can, theoretically, be stored and retrieved indefinitely. Other aspects of transmission – such as transport, transferral, reproduction and even access and search – are functions whose costs always decrease with codification. Because codified script is easy to reproduce, the number of copies can be multiplied. This makes it easier to retrieve and transport.

Considering our focus - the fragility of experiential knowledge- the highlighted function of codification that is of creating memory, communication and learning capabilities is crucial. When codifying became common, as Goody (1977: 37) writes, “no longer did the problem of memory storage dominate man’s intellectual life”. Codification generates new opportunities for knowledge reproduction. For example, a written recipe is a ‘learning programme’ enabling people who are not in direct contact with those who possess the knowledge, to reproduce it at a ‘lower’ cost. Goody (ibid: 143) writes: “The written recipe serves in part to fill the gap created by the absence of Granny, Nanna or Mémé (who has been left behind in the village, or in the town before last)”. “In part” is the important term here. Naturally, codification mutilates knowledge. Getting the written recipe does not totally eliminate the learning costs. What is expressed and recorded is not complete knowledge; it is a learning programme that helps to reproduce knowledge. When a young technician receives a user’s manual, he or she is not directly given knowledge on “how to run the machine”. That said, the manual is helpful and will serve to reduce the costs of knowledge reproduction.

As just argued, knowledge codification provides societies with stronger capabilities for memory, communication and learning. However, as for any economic operation, agents are responding to incentives: costs and benefits will explain the decision to codify, at least in the case of "codifiable but not yet codified knowledge" (Cowan et al 2000).[50] This is where price considerations come in as well as the expected private and public value of the codified form of the experiential knowledge. Viewed in this perspective, the demand for codification is influenced by a set of factors, including institutional arrangements affecting the structure of incentives for codification activities. They also concern the state of technology, which determines codification costs. This position on the endogenous nature of boundaries between tacit and codified knowledge and the importance of economic determinants is in fact very similar to that of Nelson and Winter (1982).

Thus, knowledge codification, like all other knowledge memorisation and management processes, are consequences of economic dynamics rather than their cause. So the main issues to be addressed concern not so much the mobilizing of the epistemic infrastructure or proceeding to massive codification but for the experiential knowledge to regain its vigour and strength through overcoming some of the most significant market failures which create inefficiencies in the way experiential knowledge is produced, managed, distributed and used. The main issue is for any piece of experiential knowledge to regain its former status: instruments and tools that give the individual and the community the capacity for effective action in the current socioeconomic contexts.

We will apply this framework to the particular case of traditional medical knowledge.

4.4 Traditional Knowledge

Traditional knowledge is a form of experiential knowledge that is very interesting to study given its long history and applications in many areas, including health care and use and management of resources such as land, forest, water, plant, and animals (i.e. farming practices, water, woodland, and livestock management and conservation). One of the specific characteristics of traditional knowledge is that it is developed, sustained and passed on from generation to generation within a group of people (community), often forming part of its cultural or spiritual identity.[51] Traditional

[50] The "codifiability" of knowledge depends on the existence of appropriate languages, printing technologies and modelling capabilities for the knowledge under consideration.

[51] There is no internationally agreed legal definition of traditional knowledge. Member States of the World Intellectual Property Organization (WIPO) are currently discussing the definition of traditional knowledge in the context of the

knowledge includes 'knowledge, know-how, skills, innovations or practices that are passed between generations, in a traditional context, and that form part of the traditional lifestyles of indigenous and local communities who act as their guardian or custodian."[52] It is valuable in several ways. It supports local livelihoods in addition to forming an integral part of a local culture, lifestyle, and identity. Outside the local context, traditional knowledge is also a source of knowledge for modern innovations. For example, knowledge related to the properties and use of biological resources can be of use for scientific research or for commercial development of products and services in a number of industries including food, agriculture, forestry, cosmetics, bio pesticides, pharmaceuticals, neutraceuticals, among others.

Traditional knowledge can also be *individual* or of a *collective* nature whereby it is produced, shared, known, and practised by all members of a community. Some forms of traditional knowledge, particularly that which is considered sacred (of special spiritual value) may be kept closely guarded, or practised and passed only by certain persons in the community, such a spiritual leader.

Some forms of traditional knowledge can be made *explicit* and as such are *codifiable*, while much of it is *tacit*. Explicit forms of traditional knowledge can be embodied in products such as medical remedies or in expressions such as art and crafts or remain dis-embodied (i.e. rituals or practices).

In the remaining part of this study we will focus on the specific case of *traditional medical knowledge;* a specific form of traditional knowledge that continues to be highly relevant for meeting health care needs. Some forms of traditional medicine are also being formally incorporated into national health systems alongside modern medicine. Traditional medicine can be understood as "the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental

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Intergovernmental Committee on Intellectual Property, Genetic Resources, Traditional Knowledge and Traditional Cultural Expressions (TCEs). The Convention on Biological Diversity, Art 8(j) entitled "Traditional Knowledge, Innovations and Practices" refers to "knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles".

[52] See WIPO, 'Intellectual Property and Genetic Resources, Traditional Knowledge and Traditional Cultural Expressions' (Publication No 933, 2012).

illness."[53] Some well-known forms of traditional medicine include Chinese medicine, Indian Ayurveda, Sidhha and South-Asian and Arabic Unani medicine.

In some countries traditional medicine is incorporated into the national health system (i.e. China, India) while in others some forms of traditional medicine can be considered "complementary" or "alternative" (i.e. Europe, Switzerland, United States) alongside other forms of herbal-based, non-conventional treatments that do not fall strictly under the definition of traditional medical knowledge, such as naturopathy and certain forms of manual therapies such as chiropractic or osteopathy.[54]

Traditional medicine products and complementary medicine products (T&CM) are jointly defined as by the WHO as products that "include herbs, herbal materials, herbal preparations and finished herbal products that contain parts of plants, other plant materials or combinations thereof as active ingredients. In some countries herbal medicines may contain, by tradition, natural organic or inorganic active ingredients that are not of plant origin" (WHO 2013). On the other hand, T&CM practices "include medication therapy and procedure-based health care therapies such as herbal medicines, naturopathy, acupuncture and manual therapies such as chiropractic, osteopathy as well as other related techniques including qigong, tai chi, yoga, thermal medicine and other physical, mental, spiritual and mind-body therapies" (WHO 2013).

The use of traditional medicine is associated to a number of factors, including availability (choice of alternatives), accessibility (geographical proximity for treatment, ease of practice), affordability (cost as compared to other systems of medicine) and acceptability (consumer preferences, dissatisfaction with allopathic medicine). For example, studies reveal high acceptability of traditional medicine in selected African countries (Peltzer 2009, Abdullahi 2011) and more generally in contexts where traditional medicine is closely linked with peoples' cultures (Mander et al. 2007). In developing countries, particularly in rural areas, traditional medicine can be the only form of health care available relying on local practitioners or "healers". Moreover, where the costs of traditional or complementary medicine are lower as compared to conventional medicine, it can be a source of cost savings for public health systems. Accordingly, the World Health Organization rec-

[53] http://www.who.int/medicines/areas/traditional/definitions/en/, Accessed 7 October 2014.

[54] The WHO defines "complementary medicine" and "alternative medicine" as "a broad set of health care practices that are not part of that country's own tradition or conventional medicine and are not fully integrated into the dominant health-care system. They are used interchangeably with traditional medicine in some countries." http://www.who.int/medicines/areas/traditional/definitions/en/. Accessed 7 October 2014.

ommends that countries integrate traditional medicine in national health systems to improve health outcomes - promote universal health coverage (WHO 2013).[55] Given the widespread use in developing countries, traditional medical knowledge is a relevant pre-existing knowledge base and competence that should be drawn upon to meet local health needs. It can also be developed as a source of more radical innovations (i.e. modern drugs). Currently, much of traditional medical knowledge is suffering from neglect and de-learning.

The rise in global demand for traditional and complementary medicine is one of the main factors driving the new wave of national country policies and initiatives aimed at its promotion. In 2007, approximately 38 percent of US adults aged 18 years and over and approximately 12 percent of children used some form of complementary or alternative medicine (Barnes et al. 2008). In the EU it is estimated that approximately 65% of the population have used complementary or alternative medicine (CAMDOC Alliance 2010).

From the consumer/patient perspective, a characteristic and appealing feature of traditional medicine is the holistic nature of treatment. While in allopathic medicine the emphasis is on single pills and search for cure-alls, traditional medicine stresses that individuals, given their particular constitutions (even temperament), are affected differently by disease, illness or stress/lifestyle factors, and thus respond differently to medication or treatment (EUROCAM 2012). The practitioner can alter the treatment accordingly. The focus is often to prevent illness or improve health, rather than tackle a particular pathogen/disease. This is an important characteristic of experiential knowledge for health; it is generally applied beforehand to prevent broader problems (illness) before it can occur. In this sense, it can be a useful complement to allopathic medicine, rather than an alternative. It is also appealing that traditional or complementary medicine treatments can be are less invasive, less toxic and less costly as compared to biomedical treatment with conventional drugs.

Traditional medical knowledge is also of interest as a source for potential new drug discovery based on natural products. Many modern medicines have been developed from plant sources and associated traditional medicinal knowledge, and it is increasingly possible with biotechnology and synthetic biology (Cragg and Newman 2013). It is estimated that 20–25 per cent of pharmaceutical products are derived from genetic resources, in a market that is worth US$640 billion (Greiber et

[55] See also Sixty - Seventh World Health Assembly, Resolution WHA67.18, Traditional Medicine, 24 May 2014. http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R18-en.pdf

al. 2012). There is ample evidence in different settings that leads of the properties of plants are being gathered from traditional medicine as input for new drugs in modern medicine (Calixto 2005, Singh et al. 2013).

4.4.1 Traditional medical knowledge compared to hybrid systems and biomedical knowledge

In order to understand the specificities and dynamics of traditional medical knowledge, we consider that it is relevant distinguish between *traditional* medicine, *hybrid* systems and *biomedical* medicine. These different knowledge systems can nonetheless be complementary. We refer to hybrid systems as those that combine traditional medicine and other forms of non-conventional medicine that have integrated modern medicine approaches, for example that have adapted research methods, practices or institutions of allopathic, biomedical medicine.

Table 7 summarizes features of each of these medical knowledge systems.

Table 7. Comparison of medical knowledge systems

Knowledge	*Traditional Medicine*	*Hydrid/ integrative medicine*	*Biomedical science*
Transmission	Oral mainly, tacit	Codified	Codified
Product	TM products	T&CM products	Pharmaceuticals based on natural products
Practices	TM practices, variable	T&CM practices, towards standardization	Conventional medicine practices, standardized
Practitioners	TM practitioners, i.e. spiritual leaders in villages	Accredited T&CM practitioners and conventional medicine professionals and health workers	Conventional medicine professionals and health care workers, i.e. doctors, nurses
Evidence-base, research	Low. Humanistic, symbolic	Combining humanistic and scientific	High. Scientific.
Scope	Local/national/regional	National/regional/ Global	Global

One of the particularities of traditional medical knowledge is the difficulty in ensuring its transmission. As discussed earlier, tacit knowledge is difficult to make explicit for transfer and reproduction, and it is also a costly process. Tacit knowledge is not detached from the person in possession of the knowledge, unless it is codified which is most often not the case with traditional medical knowledge. Therefore, its reproduction of depends to a large extent on the groups' social cohesion. Much of traditional medical knowledge is embedded in the specific practitioners who have acquired/learnt the experiential knowledge.

It is the case that "means of reproducing knowledge can easily fail to operate when social ties unravel, when contact is broken between older and younger generations and when professional communities lose their capacity to act in stabilising, preserving and transmitting knowledge. In such cases, reproduction grinds to a halt and the knowledge in question is in imminent danger of being lost and forgotten" (David and Foray 2003).

In traditional medical knowledge systems knowledge production and circulation evolves over time within the local context, it is not static. The community of practitioners and users are affected by changes in the ecosystem and external factors that can impact the knowledge base. Loss of knowledge and de-learning is taking place within traditional medical knowledge systems due to changing lifestyles (i.e. urbanization), as well as to increased difficulty to access to plant and other resources required for the production of medicinal products and lack of skilled practitioners to pass on know-how. Changing lifestyles can also render this prior knowledge less relevant when it can no longer be relied on to support livelihoods. Indeed, the strong role of traditional practitioners in the traditional medicine systems as compared to hybrid systems and biomedical science is a significant difference among the knowledge systems and their robustness.

Studies show there is a generational loss of traditional medicine knowledge describing the use of plants as medicines and overall diminishing knowledge and information available on medicinal knowledge of plants (Buenz 2005). This loss is also associated to the historic marginalization of traditional medical knowledge and traditional practitioners at the periphery of modern medicine due to colonial pressures and increased professionalization and regulation of traditional medicine (Ongugo et al. 2012; Davey 2013). With growing global demand for plant-based medicine, the lack of availability of quality raw materials is also considered problematic for the growth of the industry (Pardawan et at 2005).

The fact that traditional medicine continues to be used widely, even as conventional, allopathic

medicine is increasingly available, can be an indication that traditional medical knowledge and its practice is highly resilient and endures over time, despite its fragile nature. However, it should be a cause for concern that the knowledge base (residing with traditional practitioners) that is essential for the safe and effective use and practice of traditional medicine, appears to be weakening.

4.5 Medical knowledge and public health

Before we move on to discuss market failures in the domain of traditional medical knowledge, it is worth noting that the market has intrinsic limitations for the efficient allocation of resources for the production and management of medical knowledge and innovation, given the special characteristics or "ab-normal economics" in the health sector (Hsiao 1995). Not only is not possible to rely on a competitive market regime for the economically efficient generation of medical knowledge, given that is a public good, but also it is considered in many societies that allowing the market to provide medical products (diagnostics, vaccines, drugs) and services (health care) purely as private goods (purchasable on the market based on consumers' preferences and willingness to pay) is less than socially optimal. The market system does not distinguish among income levels and therefore part of the population is excluded from access when costs of goods and services are higher than can be afforded by those who are poor. Hence, there is a central government role in public health to ensure access on the basis of health needs rather than ability to pay. In this sense, medical products take on characteristics of public goods (non-exclusive and non-rival in consumption), whether they are be provided directly by the government or by private sector (under strict government regulation) or a combination of the two.

A number of governments have introduced universal health care coverage (achieved through different models of financing) for greater equity in health, whereby people can access health services independent of income. This is in line with the right to health, a fundamental human right, that every human being is entitled to the enjoyment of the highest attainable standard of physical and mental health.[56] As noted by Hsiao (1995), decisions about where government should intervene in

[56] The right to health is recognized in the 1946 Constitution of the World Health Organization, the 1948 Universal Declaration of Human Rights (UDHR), the 1966 International Convenant on Economic, Social and Cultural Rights, Article 12, and other international human right legal instruments. It is discussed in detail in the General Comment No. 14 of the United Nations Committee on Economic, Social and Cultural Rights, E/C.12/2000/4.

the market and the structure of a health sector rests on the social values that a national embraces, and these social values in turn shape policies that trade off among equity, efficiency and control of health costs.

4.6 Market failures in traditional medical knowledge

We already argued that the precious traditional institutions are coming under strain. This is particularly clear in the specific case of traditional medical knowledge, where a range of factors is contributing to the deterioration of the traditional framework. As a result, the traditional medical knowledge becomes fragile and new mechanisms are necessary to ensure its preservation, improvement and distribution. In contrast, the problems of public good, ownership, and tyranny of small decision externalities which were latent in the domain of traditional medical knowledge when the traditional institutions worked effectively are exploding today when such knowledge is subject to market dynamics. Market failures due to externalities affect firms operating in commercial markets for traditional medical products and services.

Traditional medical knowledge, as other forms of knowledge, has public good characteristics. Moreover, to address public health needs, public health policy may treat medical products as public, or quasi-public goods. In the community context where traditional medical knowledge is historically practiced, the market may not exist or otherwise not be a central institution (in the sense of organizing the production and exchange of private goods and existence of competition). Preventive and curative medical services are meant to be available to all, and in this sense take on public good characteristics, yet customary law regulates who can learn traditional medical knowledge, the process, and who can practice. Government regulation may be lacking. The system provides incentives and pay-offs to traditional knowledge practitioners that are not necessarily monetary, such as social status. Likewise, rights to the use traditional medical knowledge by community members are also recognized through customary law. Local natural resources, such as forests from where medicinal plants are sourced are also communally managed. In this sense, as advanced by E. Ostrom (1990), local communities can be effectively self-organized, much as a private association or private-club to manage the production and dissemination of traditional medical knowledge, -a local public good-, and local forests -a common-pool resource. While regulating use of medical knowledge within the community as a public good, whereby no one is excluded from en-

joying medical treatment, other communities or third parties can be excluded from enjoying those benefits.

While the weakening of traditional institutions can lead to broader knowledge diffusion within the community, it does not translate necessarily into preservation or increased practice. Some knowledge may not be readily replicable (because it is normally held and passed on orally and only by traditional practitioners, the expert and personalized nature of the practice, and reliance on use of local natural resources that may no longer be available). Moreover, some forms of traditional medical knowledge, such as knowledge considered sacred or of special spiritual value, are not available for all community members to learn or practice. In this case, there is a loss of the stewardship function that traditional practitioners play in preserving and regulating the use of knowledge based on customary law. Knowledge may also deteriorate, despite continued practice, due to lack of institutions to ensure proper learning and passing on.

Institutional change, though slow, can take place within the community in adapting to the changing context. However, to the extent that traditional medical knowledge is linked to meeting local health needs, there may be good reason for public policy involvement in institutional building. In a changing community context whereby traditional medical knowledge ceases being embedded in and supported by traditional institutions, there is a need for design of new institutions when traditional institutions fail to play the previous role. This may involve either reconstructing traditional institutions to the extent possible (i.e. through the creation of new incentives for the preservation of traditional medical knowledge through the role of traditional practitioners) or adopting new institutions.

Government, or private firms or a combination of the two, may replace the community role in the management and use of traditional medical knowledge and natural resources. Some institutions can be derived from those generally used in the domain of scientific knowledge. Codification is an important mean for the preservation of existing traditional medical knowledge and to facilitate the learning and passing on process in light of the rupture of traditional social ties.
For private firms operating in commercial markets for T&CM products and services, knowledge spillovers and free - riding by competitors due to public good externalities is a key concern. Private agents are likely to undersupply medical knowledge and produce innovations at the socially optimum level because of inability to privately appropriate benefits from knowledge production. Yet for the development of private enterprise based on traditional medicine, the solutions identified for the production of scientific knowledge, such as direct government production, subsidies, legal

monopolies (intellectual property rights), have not been applied widely to stimulate traditional knowledge production.

T&CM requires more support, notably through the allocation of financial resources for more codification and research. In the case of plant-based products, there are significant costs that T&CM firms need to make to meet increasingly stringent regulatory standards, particularly in lucrative markets (i.e. Europe, United States) prior to commercialization. Financial support by government to T&CM currently is minimal as compared to financing for scientific-based medicine. For example, the US National Center for Complementary and Alternative Medicine had a budget of approximately USD $124 million, compared to the overall budget of the US National Institutes of Health of approximately USD $25 billion in 2013.[57] The role of intellectual property in relation to the public goods problem is discussed in detail in Section 4.6.

As in the case of public good externalities, in the local community context traditional institutions address the potential problem of ownership externalities. On the other hand, under market conditions, one can clearly see how ownership externalities apply to the case of traditional medical knowledge. It is difficult to observe, measure and adequately assess its value for society, beyond the rising market value for some T&CM products and services. Despite reported benefits of traditional and complementary medicine, the endorsement of its use for public health is subject to significant scepticism from policy makers and the scientific medical community. This is due to the limited evidence-based scientific analysis of the quality, safety and efficacy of treatment and practice. As compared to modern, science-based medicine, it is only recently that formal institutions are being created to evaluate and regulate the use of traditional medicine products, and to attest and validate the know-how and qualifications of self-declared practitioners.

These are certainly legitimate concerns but they also reflect unfamiliarity and understanding of traditional knowledge systems. For most conventional medical authorities and practitioners it is difficult to evaluate the value of knowledge outside their own framework for evaluation that is part of the science-based knowledge system, and thus there is enormous scepticism among the scientific community on the value of traditional medical knowledge.

This is in fact the case with all experiential knowledge and a source of its fragility but at the same time of its value; it is grounded on experience obtained through its continued use over long periods of time. Given that the evidence and research-base of traditional medical knowledge is

[57] See http://report.nih.gov/categorical_spending.aspx.

largely observational rather than scientific, and that it is regulated through informal traditional mechanisms, it is not considered reliable, pending evaluation, from the scientific-approaches applied in biomedicine. Consequently, increasingly science-based approaches are being applied to traditional medical products and practices for their examination and prior to authorizing their formal use. However, the characteristics of traditional medical knowledge pose unique problems in this integration with modern science. The diversity of practices of traditional medicine among countries or even among practitioners is a challenge for ensuring quality and efficacy and for establishing harmonized standards of production and practices through regulation.

The personalized character of traditional medicine also poses particular challenges for the production of modern drugs based on such knowledge, for example for carrying out randomized controlled trials. Traditional medicine is thus a difficult subject for scientific, evidence-base evaluation. Nonetheless, this is the approach that countries are increasingly adopting where traditional or complementary medicine is practiced, where there is an interest in promoting its export. It is also the policy approach that is being advanced by the WHO. Efforts are being made to increase uniformity in the processes of production, ingredients and final products to ensure more homogeny in formulations. However, it is also worth noting that these efforts can also clash with the personalized and holistic character of traditional medicine, putting stress on some of its key attributes and appeal.

The public health challenge remains to increase research to improve the safety and efficacy of treatments based on T&CM products and practices to meet health needs, both in the local context where it is most frequently used as a source of health care and as part of national health systems, while preserving the nature of traditional medical interventions. Supportive forms of evidence-based research include experiential research that is well - suited for experiential knowledge. However, science-based approaches would serve to provide broader validity to T&CM. These include comprehensive toxicity studies of traditional medicinal plants and clinical trials of single plants or remedies containing mixtures of plants (Jäger 2005). Efforts also need to be made to ensure the qualifications of practitioners, such as through accreditation systems overseen by government institutions in an effort to integrate traditional practitioners who hold tacit know-how into national health systems, rather than creating only new categories of professionals in the practice of traditional medicine that breaks the link to the historic learning process of traditional medical knowledge through inter-generational passing on.

In the local community context, where traditional medical knowledge and local natural resources is managed through customary law, the problem of the suboptimal effect of small decisions in terms of size, scope and time perspective – the tyranny of small decisions- is avoided. In the context of market dynamics for T&CM, however, the problem is evident. A clear example is the sustainability and proper use of plant-based traditional medicinal products. Firms, T&CM practitioners and consumers are increasingly using medicinal plants (as evidenced by the growth of the market) with little concern on the overall impact of their individual decisions on the long-term sustainability of such use. Issues such as the generic erosion among wild plants and decreased quality of raw materials are not internalized in such "small decisions". For example, due to increased demand of plant-based medicines, and the increasing lack of access by traditional practitioners (or other sellers) to native plant resources as raw material, in certain contexts these are resorting to substituting these in preparations with common plants (also passed off intentionally in the market as native plant-based medicines), posing health risks for users (Shanley and Luz 2003).

Hence, higher-level decision-making may be necessary to address these and related "macro" problems. Some of the higher-level policy actions that can be taken to ensure supply and processing of raw materials of good quality in a sustainable manner are introducing sustainable practices for the collection, cultivation and harvesting of medicinal plants; introduce quality controls mechanisms for monitoring products sold in the market; design of a conservation strategy for threatened species and for the preservation of traditional medical knowledge.

The technical guidelines relating to the quality control of medicinal plants developed by the WHO - Guidelines on Good Agricultural and collection practices (GACP) – are an example of higher-level decision making to address this type of externality.

4.7 Institution building to support traditional medical knowledge

In this section we take a closer look at the institutions that underpin traditional medicine as compared to those of hybrid and science-based medicine, and consider the extent to traditional institutions are evolving in themselves in light of the changing local context and whether this process sufficient, or otherwise what should be the new institutional design for what cannot be rebuilt of the traditional institutional framework. In doing so, we consider to what extent institutions that support scientific knowledge can be extended to accommodate traditional medical knowledge.

Science-based medicine has developed mechanisms to support the creation, codification and circulation of scientific know-how that are largely absent for traditional medical knowledge.

Table 8 provides a comparison between selected institutions in traditional, hybrid and biomedical medical systems.

It is now well established in economics and other social sciences that the analysis of institutions, in our case those that backing different forms of medical knowledge and their practice, is as important exercise. Institutions can be broadly defined as the prescriptions that humans use to organize all forms of repetitive and structured interactions including those within communities, markets, firms, and governments (Ostrom 2005). They consist of both informal constraints such as sanctions, customs and codes of conduct, and formal rules, such as laws and property rights (North 1990). Underlying institutions are assumptions, values and preferences that drive human behaviour and decision-making. These help to understand how the formal institutions - rules of the game- were formed, how they change and why they may or may not allow the outcomes that were expected. Institutional choices also underscore the legitimacy that is given to the system.

Institutions historically underlying traditional medicine are undergoing significant change and weakening to various extents in different settings. These remain stronger in settings where the influence of biomedicine (or access to modern medical facilities) is less prevalent.

These include institutions that regulate the use, transfer and reproduction of knowledge, such as community customary laws that provide a means for knowledge transmission based on kinship or other defined criteria and differentiate legitimate practitioners from “quacks”. As previously noted, we observe that a cause for the deterioration of traditional medical knowledge (and in consequence the reliability of products and practices) is the weakening of the historically close connection between the traditional medical knowledge of practitioners and their knowledge of the local context (i.e. the local people, lifestyles and culture, uses of local plant resources for medical preparations).

The extensive experience of practitioners in relation to a specific context is what traditionally constitutes the evidence-base that supports the practice of traditional medicine by such “experts”. The knowledge is then passed on from generation to generation. Thus, the transfer and reproduction of useful traditional medical knowledge cannot, without problems, be disconnected from the knowledge and skill derived from long-term experience gained in a specific, local context.

Table 8. Institutional diversity among medical knowledge systems

Knowledge	*Traditional Medicine*	*Hydrid systems*	*Biomedical science*
Type of Institutions	Informal	Informal and formal	Formal
Knowledge validation, transfer and reproduction	Inter-generational passing on by TM practitioners to eligible apprentice (i.e. status within the community). Learning by doing.	Accreditation mechanisms for existing T&CM practitioners (i.e. registers, associations). Formal training or education system, hybrid universities.	Formal education system, universities. Formal research and development.
Government financial support	Low.	Low.	Strong. Significant budget to institutions to support basic research.
Regulation	Customary law. Un-official. Highly variable among countries.	Increasingly regulated at national/regional level. Variable among countries.	Strong. Harmonization.
Intellectual property law	Use of IPRs is uncommon. Measures to counter misappropriation / erroneous grant of IPRs over known TM uses of plants and TM practices and support compliance with national ABS laws.	Efforts to adapt IPRs to T&CM specificities and use IPRs. Measures to counter misappropriation / erroneous grant of IPRs over known T&CM uses of plants and T&CM practices and compliance with national ABS laws.	Use of IPRs to protect/secure financial gain from commercialization of innovations involving use of plant resources and associated TM knowledge.
Access and benefit sharing law	Countries and/or TM practitioners may condition the access/use of plant resources and associated TM knowledge by third parties to prior informed consent and mutually agreed terms for the sharing of the benefits that may derive from commercialization of innovations based on these.	Applicable with respect to TM.	Compliance with national ABS laws can be required for access and/or use of plant resources and associated TM knowledge and for the commercialization of innovations based on these.

Such disconnection may alter its relevance and even dangerously increase the potential risks of the treatment. For example, it has been shown that certain traditional medicine treatments can have interactions (i.e. side effects, toxicity) when used in conjunction with pharmaceutical drugs (Peltzer et al. 2008).

Another important source of weakening of traditional institutions is the increased reliance on and preference for modern biomedicine, as evidenced by the continued exclusion of traditional medicine from most national health systems. Thus, there has been lack of sufficient government support for the strengthening of institutions to support traditional medical knowledge. Moreover, it appears that while a growing number of firms and government policies aim to develop T&CM, reaching new profitable global markets appears to be the main focus, with less emphasis on addressing national health needs. The intensified search for validation of T&CM beyond the local setting explains why biomedical thinking is increasingly dominant in T&CM medicine, particularly in Western countries, along with efforts to standardize practices according to scientific methods. Thus, much of current debate on the value of traditional, alternative or complementary medicine rests on different perceptions on the validity of the underlying institutions, both formal and informal.

The forms of evidence and means for the transmission of knowledge that are considered as adequate and reliable in biomedical science for ensuring safety and efficacy of the products and practices are for the most part absent in traditional medicine systems, the latter relying on intergenerational relations and long term clinical practice. Conversely, in traditional medical systems include measures of efficacy that may be relevant for health care and yet less prominent in biomedicine, such as patient perceptions of health, change in lifestyle, and other non-scientific evidence that the treatment is effective. Growing compliance with the norms of modern bioscience in relation to use of traditional medicine is evidenced in countries such as Brazil, India and China where traditional medicine has long been practiced (Menon et al. 2010). It is less clear whether such efforts are aimed at promoting traditional medical knowledge use to address domestic health care priorities or mainly focused on promoting the use traditional medical knowledge for leads into the development of new biomedical products. The WHO is leading efforts for regulating traditional medicine, as part of an overall trend to develop regional/global regulatory mechanisms for regulating herbal drugs. For example, the European Directive 2004/24/EC introduced a simplified registration procedure for traditional herbal medicinal products toward harmonizing the current legislation framework for all herbal medicinal products in the European Union (EU). Fulfilling the

requirements for the registration of non-European traditional herbal medicinal products within the EU remains a challenge for most firms, as requirements include demonstrating a 15-year minimum medicinal use period in the EU and evidence of absence of health risk (Qu et al. 2014). Thus, understandably much of the efforts of firms seeking new markets abroad are focused on meeting this type of regulatory requirements.

The concerns on the quality, safety and efficacy of T&CM products and practices and the lack of assessment of the knowledge and qualifications of traditional practitioners are often well founded. This situation can dangerously undermine the integration of T&CM into formal health care systems, in addition to impeding the entry of traditional medical products into global markets. Accordingly, institutions do need to be re-designed or established to address these concerns. In addition, as we have advanced in this study, there is a notable gap in institutions to support the production and continued transmission of traditional medical knowledge given market failures, as compared to biomedical knowledge. The challenge, then, is to design and sustain institutions to support traditional medical knowledge with clearly defined policy objectives and understanding that these will impact the outcomes differently depending on the setting.

For the most part, the institutions advanced to support traditional medical knowledge are an extension of those of biomedicine, as promoted in the WHO Traditional Medicine Strategy 2014-2023 (World Health Organization 2013). These include, in addition to uniform regulations for products and practices, bodies for the accreditation/registration of existing practitioners (associations), institutions for the uniform education/training of practitioners (training institutes, universities), direct financing of knowledge production, application of science-based tools such as qualitative research methods and data gathering and analysis and intellectual property rights. However, not all institutions of scientific knowledge can be readily extended to traditional medicine systems. Some of the institutions developed to promote the production and diffusion of scientific knowledge can be adapted and others may not be suitable.

Table 8 describes how institutions such as intellectual property (IP) laws and access and benefit sharing (ABS) laws have different outcomes among various medical knowledge systems. In Section 4.8, we discuss these institutions in more detail.

4.8 Intellectual property rights and access and benefit sharing

IP law is a well-established institution within science-based knowledge systems. In contrast, it is largely absent in traditional medical knowledge systems. The State-grant of intellectual property rights (IPRs) as legal rights to exclude others from use of knowledge goods is a policy tool that is usually used in the context of promoting knowledge production. Patents, Trademarks, copyrights, geographical indications and plant variety protection are some of the various forms of IPRs. They are widely used by firms and individuals to appropriate returns from their innovations or other creations and to deter imitation. Incentive mechanisms are also needed for the continued production and dissemination of traditional medical knowledge. Therefore, it is relevant to examine the extent to which IPRs are a relevant institution.

The grant of IPRs involves an important knowledge trade-off. On the one hand, the free sharing and rapid dissemination of traditional knowledge is socially beneficial to access the knowledge and expand its use in the health system and towards the aim of universal health care. The ability of IPR holders to legally exclude others from the use of protected products can be detrimental for the dissemination and access to traditional medical knowledge and products by people who cannot afford to pay high prices. On the other hand, private firms involved in producing traditional medicine products will seek mechanisms for the private capture of the benefits from the economic use of the knowledge, given that spillovers can deter private investment. Hence, in managing the knowledge trade-off between access and incentives, a central policy question is how to ensure the preservation of traditional medical knowledge and encourage production of new useful medical products and practices based on such knowledge. The policy approach may vary depending on the defined priorities. As part of health care in poorer countries, ensuring access to treatments is a key criterion. In this case, alternative incentive mechanisms may need to be crafted, such as increased government financing to research and knowledge transfer institutions that incorporate traditional practitioners, support for associations, and public-private partnerships and other mechanisms that de-link medical innovations from high prices, as discussed in Chapter 2. Conversely, if priority is given to the economic exploitation of traditional medical knowledge and response to the growing global demand for T&CM products and practices in profitable markets, mechanisms such as IPRs to allow private capture of benefits from exploitation of knowledge may be relevant.

A controversial aspect of IP law is the fact that it allows for the privately appropriation of innovations that are based on traditional medical knowledge, without any compensation or benefits from the innovation directly accruing to the traditional knowledge holders (such as a community of traditional practitioners).

Traditional knowledge that is disclosed in written, oral, or any form is most often considered by the IP system to be in the 'public domain', that is, free for anyone to use. In the case of patents, proper examination of patent applications should reveal the traditional knowledge that has been disclosed to society (in the public domain) as "prior art" – previously existing public knowledge, and on this basis the patent should be rejected. When this is not the case and a patent is granted, it may be very costly and difficult for traditional knowledge holders to challenge a granted patent. For example, a large number of patents granted over plant biological resources for uses that have long been known and practised in traditional medical systems, for instance Ayahuasca, Turmeric and Neem. This is a situation often described as 'biopiracy' or misappropriation of traditional knowledge by the patent system.

Efforts to improve prior art searches for traditional knowledge in the public domain include increased codification of existing medical knowledge and making it more readily available to patent offices in multiple languages to assist in their examination of patent applications. An example of a database of traditional medical knowledge is the Indian TK Digital Library.

Traditional knowledge that is not meant to be disclosed (i.e. secret or held only by a practitioner or community) can also in most situations be legally incorporated in an innovation for which IPR protection is claimed, without consent or compensation of the original holder of the traditional knowledge. In both instances, patents are granted in relation to disclosed or undisclosed traditional knowledge create situations whereby the patented product or process may not be used and exploited by others, including by the original traditional knowledge holders.

A second type of situations that raise concerns over the impact of the IP system on traditional medical knowledge relates to the application of rules on access and benefit sharing (ABS) with respect to traditional knowledge associated to plant and animal biological resources.[58] The condi-

[58] Countries that are party to the Convention of Biological Diversity (CBD) and the Nagoya Protocol are legally bound to the defined rules on access and benefit sharing, whether they are users or providers of biological resources and/or associated traditional knowledge, or both. Nonetheless, there is a high degree of variability among countries as to whether and how they regulate access and use of biological resources and associated traditional knowledge. See http://www.cbd.int/abs/default.shtml.

tions for the grant of IPRs are normally determined solely by the IP laws. However, it may be the case that countries which have adopted national ABS laws establish requirements for the legal access and use of biological resources and associated traditional knowledge, such as requiring the prior informed consent (PIC) of the traditional knowledge holder (i.e. traditional practitioner) or designated government authority and/or the sharing of benefits (economic or some other form of agreed compensation) from the innovations that may be derived from the use of the biological product and associated traditional knowledge. National ABS laws may also require that prior to the grant of an IPR the applicant shows compliance with the PIC and ABS requirements.

An additional source of tension in the application of IP laws over traditional medical knowledge is the fact that in certain settings customary laws and practices may regulate traditional medical knowledge production and use, yet the rights provided for under customary laws are not recognized in national legal systems (for example rules on practice of traditional knowledge by only select members of the community). Moreover, IP laws generally exclude traditional knowledge as a potential subject matter of protection.

Significant policy debate and academic attention has been given to the question of whether the use of IP tools should be promoted to protect innovations and creations that stem from within traditional knowledge. In principle, traditional knowledge is a creation of the human mind, and therefore can be protected by IPRs. However, it does not fit easily within the IP system. This is because of the specific characteristics of traditional knowledge (i.e. collectively held makes it difficult to identify who the IPR can be attributed to, it is passed on from generation to generation rather than novel). Moreover, prescriptions and concepts of the IP system can alien to traditional knowledge systems and hence may be inappropriate or incompatible with their beliefs and practices.

Existing IP tools to some extent can be useful and are being used in practice to provide protection to traditional knowledge and promote traditional knowledge-based innovations. For example, patents can be granted to traditional knowledge based innovations provided they meet the patentability requirements of novelty, inventiveness and industrial applicability. Trademarks, certification, and collective marks, and geographical indications can be used to market products issued out of traditional knowledge based innovations and to protect the reputation and goodwill associated with the traditional knowledge. The law of unfair competition, including passing off, can be used to prevent various forms of misrepresentation as well as false endorsement claims. Finally, trade secrets law can protect undisclosed information. In some instances, conventional IP laws have also been adapted to provide some form of protection to traditional knowledge. However, it is difficult

for traditional knowledge holders to use the IP system. Some of the difficulties they face in practice include meeting the criteria for IP protection and costs of access to the system (fees, transaction costs). Moreover, in cases where IP protection is gained, traditional knowledge holders may still face enormous difficulties in the commercialization of their innovations and their enforcement against third parties. The shortcomings in existing and adapted IP laws have prompted some countries and regions to set up sui generis systems (a system of its own) to cater to the unique character of traditional knowledge. At the international level, negotiations are underway within the World Intellectual Property Organization (WIPO).[59]

4.9 Conclusions

Traditional medical knowledge is a form of experiential knowledge that is of value to address health needs. In the absence of traditional institutions that served to support traditional medical knowledge reproduction and transmission, such knowledge becomes fragile and is more likely to suffer from deterioration or even disappearance, as compared to scientific knowledge. The loss of traditional medical knowledge leads to reduced capacity for effective action in certain socioeconomic contexts and circumstances in which such knowledge was previously useful.

We discussed various types of externalities that cause market failure in the context of the production and management of knowledge. We find that these externalities are not well corrected for in the specific case of traditional medical knowledge, in contexts where the exchange of traditional medicine products and services are organized through markets, as is increasingly the case, and on a global scale to meet health needs beyond the local context and exploit for-profit opportunities.

In contrast, market failures do not arise in the local community context, when knowledge and natural resources are effectively managed by the community and supported by traditional institutions. When the community system is in strain, there is increased risk of deterioration and loss of traditional medical knowledge and its ability to be put to use to meet local health needs. Thus, the

[59] Sui generis frameworks may be inspired in IP concepts that are extended to the particularities of TK innovations or aim to provide a more holistic approach to the protection of TK, for example building upon customary law. Other approaches have also been advanced, for example, to develop a compensatory liability regime that would give TK innovators compensation for a limited time period rather than exclusive rights as in the IP approach.

preservation of local community contexts and traditional institutions should be supported by government policy to the extent possible.

Where this is no longer achievable, attention should be given to new institutional design and integration with science-based institutions that work effectively to support biomedical knowledge. Science-based medicine has developed institutions and incentive mechanisms to support the creation, codification and circulation of scientific know-how. These are largely absent for traditional medical knowledge. However, institutions of biomedical knowledge cannot be readily copied for traditional medicine and hybrid systems.

Greater government support is needed towards institution building to preserve and promote traditional medical knowledge. The challenge is to design and sustain institutions to support traditional medical knowledge with clearly defined policy objectives and understanding that these will impact the outcomes differently depending on the socio-economic setting.

Strengthening and building institutions to support the production and transmission of traditional medical knowledge needs to increase attention to the local context linkage, as opposed to seeking universal solutions. Moreover, institutions need to stimulate collaborative relationships among traditional practitioners and health authorities and biomedical researchers, particularly in settings where traditional medicine is already practiced widely and the aim is to further its integration in the national health systems. The lack of proper incorporation of traditional practitioners into new hybrid institutions increases the risk of deterioration of traditional medical knowledge as well as of misdiagnosis and improper medical treatment by any type of practitioner.

It is also critical to build appropriate institutions to promote knowledge production and address the problem of externalities, while managing the often complex interactions among traditional medical knowledge holders and the diversity of users of traditional medical knowledge (i.e. researchers, firms) so as to reduce the uncertainties that surround knowledge sharing. There are important tensions in the interaction of science-based biomedical systems and traditional medical knowledge systems that inhibit useful knowledge transfers from taking place in a manner considered legitimate, as described in the relationship of IP laws and ABS laws. Governments are the responsible agents for introducing institutions that can effectively manage these tensions.

Conclusion

This study explored three interrelated themes from the perspective of economics of innovation. The first is the phenomenom of the emergence of a new form of institution – PDP – that aims to facilitate and drive R&D and innovation in the area of neglected diseases. These self-governing, private non-profit organizations are a very interesting example of institutional experimentation to provide effective solutions to a challenging innovation problem. PDPs are undoubtedly contributing to reducing the dearth of R&D and innovation in relation to neglected diseases by providing an alternative mean to undertake medical product development. It is distinct from the classical approach where private for-profit firms are at the centre of R&D activities and in bringing about innovations to market, supported by public incentive structures including public financing for R&D and strong IPRs. In the case of neglected diseases, traditional incentive mechanisms do not work well to drive private for-profit investment. PDPs are helping to fill this gap, addressing some of the major causes of market failure for R&D and innovation in neglected diseases. They mobilize public and philanthropic financing, thereby allowing costs of R&D to be de-linked from the prices of medical products, and act as "system integrators" that leverage the resources and capabilities of a diverse network of public, philanthropic and private sector partnerships. There is also evidence of success of PDPs in bringing about new medical products, although the majority are improvements or new uses for existing medical products.

The PDP institution however, also presents several drawbacks that would be worth exploring in further detail in future research. In particular, it will be useful to observe how PDPs evolve with respect to the limitations identified in this research given that the future of the PDP landscape remains uncertain. Some of the limitations identified in this study that merit further analysis are the challenges of ensuring sustainable long-term financing due to reliance on donor and public sector moneys, their policies on critical issues such as access and IPRs, coordination problems and potential duplicative efforts and competition among PDPs due to limited sources of financing, as well as insufficient transparency in PDP operations particularly in contractual terms with partners.

Another aspect is to further explore the spillover effects that PDP activities appear to have created, such as fostering greater interest and openness in collaboration and information sharing among various actors to advance R&D and innovation, particularly in the pre-competitive stage of discovery for new medicines. While in the area of neglected diseases this collaboration is largely devoid of competitive market pressures, there are indications that there is interest to further such collaborations in other more "lucrative" areas, such as for addressing market failures in the area of anti-microbial resistance. Finally, it would be useful to explore in more detail other institutional experiments, in addition to PDPs, to develop medical products as public goods to ensure dissemination and access to all populations models of innovation, that de-link the costs of R&D and innovation from the prices of medical products in the area of neglected diseases and beyond, such as the discussion in the WHO for an inter-governmental or multi-stakeholder agreement establishing mechanisms to increase global coordination of priority-setting for R&D and resource allocation for innovation based on global public health needs.

A second interrelated theme explored in this study was how PDPs, as private non-profit institutions, relate to the incentive mechanism of IPRs that firms in medical product development make significant use of and consider highly valuable to their for-profit objectives. This study contributed to a broader understanding of the role of IPRs in non-profit innovation, that is a subject that has received very little attention in the field of economics more broadly and in particular in economics of innovation.

The study finds that IPRs generally do not act as an incentive for R&D and innovation in private, non-profit institutions, taking the example of PDPs, in the same sense as IPRs are expected to do so for private, profit-maximizing firms. This is because PDPs do not seek to re-coup investments in R&D and innovation from profit margins on sales of medical products. However, the management of IPR more broadly is an activity of relative importance for PDPs, as potential "users" of background IPRs held by third parties over technology, data or know-how that the PDP seeks to access.

Contrary to the expected results, PDPs are also "producers" of IPRs, seeking to protect innovations from unauthorized use by third parties. However, contrary to for-profit firms, PDPs do so in order to advance their not-for-profit and access mandate, in particular in managing the number of collaborations they undertake with partners in R&D projects. However, this study finds that there is insufficient transparency of the terms of the agreements of PDPs with partners concerning the use of IPRs. This limitation inhibits proper assessment of the IPR management strategies of PDPs, in accordance to their non-profit and access mandates.

An important conclusion from this study is the need for a change in approach in the research on the effects of IPRs in the field of economics. The economic analysis of IPRs tends to study the social and economic effects of IPRs disconnected from the analysis of the institution that produces and manages them. However, as demonstrated in this study, the effect of IPRs is not static. Rather, the impact of IPRs and their function can vary significantly depending on the institutional context in which it is used and for what purpose. The effects of IPRs need to be linked to the analysis of the nature of the institution managing them.

The third and final theme explored in this study was traditional medical knowledge, as a form of experiential knowledge that is of value to address health needs. The study finds that as in the case of other forms of knowledge, particularly scientific knowledge, institutions are necessary to support the reproduction and transmission of knowledge.

In the absence of traditional institutions that served to support traditional medical knowledge reproduction and transmission, such knowledge becomes fragile and is more likely to suffer from deterioration or even disappearance, as compared to scientific knowledge. The loss of traditional medical knowledge leads to reduced capacity for effective action in certain socioeconomic contexts and circumstances in which such knowledge was previously useful.

Various types of externalities cause market failure in the context of the production and management of any form of knowledge. The study identifies that with regards to traditional medical knowledge, market failures do not arise in the local community context, when knowledge and natural resources are effectively managed by the community and supported by traditional institutions. However, in the specific case of traditional medical knowledge, when the community system is in strain, the traditional institutions stop operating well enough to support continous knowledge production and dissemination and to correct market failures. In this context, traditional medical knowledge suffers deterioration and may lose its relevance towards meeting local health needs. Thus, the study finds that an important mean to support traditional medical knowledge is through the preservation of local community contexts and traditional institutions.

When this is no longer achievable, attention should be given to new institutional design and integration with science-based institutions that work effectively to support biomedical knowledge. These institutions are largely absent for traditional medical knowledge. However, the study cautions that institutions of biomedical knowledge cannot be readily copied for traditional medicine

and hybrid systems. There are important tensions in the interaction of science-based biomedical systems and traditional medical knowledge systems that inhibit useful knowledge transfers from taking place in a manner considered legitimate, as described in the relationship of IP laws and ABS laws. Governments should work in close collaboration with traditional medical knowledge holders to design institutions that can effectively manage these tensions in accordance to the local social and economic context. Further research should be geared towards improving the understanding of the potential for integrating scientific knowledge with traditional medical knowledge, and the extent to which institutions associated to scientific knowledge can be adapted or improved towards supporting traditional medical knowledge.

Appendix

Chapter 2

Table 9. Medical products developed by PDPs

PDP	Innovation type	Description	Disease	Region Target	Year	Partners
DNDi	Combination therapy	NECT - Nifurtimox-Eflornithine co-administration Reduces the number of eflornithine infusions needed, has a higher cure rate than eflornithine alone and fewer severe adverse events. Cost of treatment is lower, simpler to administer and more adapted to field conditions where it is used.	HAT	Africa	2009	Médecins Sans Frontières (MSF); Swiss Tropical and Public Health Institute (Swiss TPH); National Trypanosomiasis Control Programmes of the Republic of Congo and the Democratic Republic of the Congo (DRC) (WHO), with drugs donated by Sanofi and Bayer Schering Pharma AG.
DNDi	Combination therapy	SSG&PM co-administration Combination of sodium stibugluconate (SSG) and PM. As efficacious as single-dose SSG, with the advantage of being shorter course, therefore lessening the burden on health systems, and more cost-effective.	VL	East Africa	2010	Kenya Medical Research Institute (KEMRI), Kenya; Institute of Endemic Diseases (IED), University of Khartoum, Sudan; Addis Ababa University, Ethiopia; University of Makerere, Uganda; Ministries of Health of Sudan, Kenya, and Uganda; Médecins Sans Frontières (MSF); i+ solutions, IDA Foundation The Netherlands; GLAND Pharma and OneWorld Health (OWH), USA; LEAP (Leishmaniasis East Africa Platform) The London School of Hygiene and Tropical Medicine (LSHTM).

DNDi	Combination therapy	New VL Treatments Single dose AmBisome® 10mg/kg and three drug combination therapies based on AmBisome®, miltefosine, and paromomycin (miltefosine-paromomycin, AmBisome®-miltefosine, AmBisome®-paromomycin) Currently effectiveness studies are being carried out in South Asia to demonstrate feasibility in implementing the new treatment modalities recommended by WHO (miltefosine-paromomycin, AmBisome®-miltefosine, AmBisome®-paromomycin, AmBisome® 10mg/kg) in primary healthcare settings in India with a view to extending their use in the region.	VL	South Asia	2011	INDIA: National Vector Borne Disease Control Programme (NVBDCP), Indian Medical Research Council (ICMR), Delhi; Rajendra Memorial Research Institute of Medical Sciences (RMRIMSI), Patna, Bihar State Health Society (BSHS); Médecins Sans Frontières (MSF), Spain. BANGLADESH: Ministry of Health, International Centre for Diarrhoeal Disease Research (ICDDR, B), Dhaka; Shaheed Suhrawardy Medical College and Hospital (ShSMC), Dhaka; Community Based Medical College (CBMC), Mymensingh. USA: One World Health (OWH), San Francisco. University of Tokyo, Japan; Institute Tropical Medicine-Antwerp, Belgium; LSHTM, UK; WHO Special Programme for Research and Training in Tropical Diseases (TDR)
DNDi	Formulation	Paediatric dosage form of Benznidazole New paediatric dosage formulation and dosing regimen of Benznidazole.	Chagas	Latin America	2011	Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE), Brazil; Hospital de Niños Ricardo Gutierrez, Argentina; Instituto Nacional de Parasitología, Dr M Fatala Chabén, Argentina; Hospital de Niños de Jujuy, Argentina; Ministério de Salud, Província de Jujuy, Argentina; Hospital Público Materno Infantil – Salta, Argentina; Centro de Chagas y Patologia Regional, Hopital Independencia, Santiago del Estero, Argentina: Centro de Chagas y Patologia Regional, Argentina; CONICET/INGEBI, Argentina; Centro Nacional de Diagnóstico e Investigación de Endemo-epidemias (CeNDIE), Ministry of Health, Argentina; University of Liverpool, UK; NUDFAC, Brazil

DNDi	Combination therapy	ASAQ – Fixed-Dose Artesunate/Amodiaquine fixed-dose combination (FDC) of artesunate (AS) and amodiaquine (AQ) Easy dosaging, based on four, optimized age-specific regimens. Less expensive than all other fixed-dose combinations containing artemisinin derivatives. No patent.	Malaria	Africa	2007	Sanofi, France; MMV, Switzerland; AEDES, Belgium; Zenufa, Tanzania; National Centre for Research and Development on Malaria, Burkina Faso; Universiti Sains Malaysia; University of Oxford, UK; Institute of Research for Development (IRD), Senegal; Université de Bordeaux, Faculté de Pharmacie, France; Mahidol University, Thailand; Bertin Pharma, France; Médecins Sans Frontières/Doctors without Borders (MSF); Epicentre, France; WHO-TDR; Kenya Medical Research Institute (KEMRI), Kenya ; Indian Council of Medical Research (ICMR), India; National Malaria Control Programme, Ministry of Health, Sierra Leone; Komfo Anyoke Teaching Horpital (KATHI), Ghana
DNDi	Combination therapy	ASMQ – Fixed-Dose Artesunate/Mefloquine Used in the field for many years, the combination of artesunate (AS) and mefloquine (MQ) is one of the five ACTs recommended by WHO for the treatment of uncomplicated P. falciparum malaria, preferably as a fixed dose combination. Easy-to-use treatment regimen with one single daily dose of one or two tablets to be taken over three days. 3 presentations of ASMQ are available for children; tablets are small and easily crushable. Developed in Brazil – Farmanguinos/Fiocruz.	Malaria	South East Asia, Latin America	2008	Industrial partners: Farmanguinhos, Brazil; Cipla, India. Other partners: Shoklo Malaria Research Unit, Thailand; Universiti Sains Malaysia; University of Oxford, UK; TDR; Indian Council of Medical Research (ICMR), India; Epicentre, France; National Institute of Medical Research, Tanzania; Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland; Kenya Medical Research Institute (KEMRI), Kenya; Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso; Medicines for Malaria Venture (MMV), Switzerland
MMV	Combination therapy	Coartem® Dispersible (artemether-lumefantrine) (Approved by regulatory authority (Swissmedic) and WHO Prequalified) The first high-quality artemisinin combination therapy (ACT) formulated especially for children. Coartem® *Dispersible* contains a fixed-dose combination of artemether (20mg) and lumefantrine (120mg) for the treatment of acute uncomplicated *P. falciparum* malaria.	Malaria	Endemic countries	2009	Novartis Pharma, Switzerland
MMV	Existing product received prequalification	Artesunate injection (WHO prequalified) Superiority of artesunate injection over quinine injection as first-line treatment for patients with severe malaria.	Malaria	Endemic countries	2010	Guilin Pharmaceutical Co. Ltd., China
MMV	Combination therapy	Eurartesim® (dihydroartemisinin-piperaquine DHA/PQP) (Approved by regulatory authority (EMA)) A fixed-dose combination of dihydroartemisinin-piperaquine (DHA/PQP) for the treatment of uncomplicated *P. falciparum* malaria.	Malaria	Endemic countries	2011	Sigma-Tau Industrie Farmaceutiche Riunite, Italy

MMV	Combination therapy	Pyramax® (pyronaridine-artesunate(Approved by regulatory authority (EMA) A fixed-dose combination of pyronaridine and artesunate.	Malaria	sub-Saharan Africa, South-east Asia and India	2012	University of Iowa, IA, USA; Shin Poong Pharmaceuticals, South Korea
MMV	Combination therapy	Sulfadoxine-pyrimethamine + amodiaquine (SP+AQ) (Working towards WHO Prequalification) Sulfadoxine-pyrimethamine and amodiaquine (SP+AQ) once a month for 4 months for children during the malaria season for prevention.	Malaria	Endemic countries	2012	Guilin Pharmaceutical Co. Ltd., China
FIND	Diagnostic	SD BIOLINE HAT First rapid test to screen for sleeping sickness This cheap and very simple-to-use test can be performed by health workers with minimal training, using fresh blood from a finger prick, and the results are obtained after only 15 minutes.	HAT	Angola, the DRC and the Central African Republic	2012	FIND and the Institute of Tropical Medicine (Belgium), MicroCoat Biotechnologie GmbH (Germany), the International Livestock Research Institute (Kenya), the Institute of Tropical Neurology (France), Médecins sans Frontières (Spain), the National HAT Control Programme of the DRC (PNLTHA, Democratic Republic of the Congo), the Centrafrican Institute of Agronomical Research (Central African Republic), the World Health Organization and Standard Diagnostics, Inc. (Republic of Korea).
FIND	Diagnostic	Liquid culture and drug susceptibility testing Mycobacterium Growth Indicator Tube (MGIT) and drug susceptibility testing (DST) A Mycobacterium Growth Indicator Tube (MGIT) and drug susceptibility testing (DST).	TB	Endemic countries	2007	Becton, Dickinson and Company (BD), United States
FIND	Diagnostic	Rapid Speciation for MDR / TB Capilia TB test A Capilia TB test. Simple, fast (15 minute) detection of TB.	TB	Endemic countries	2007	Tauns Co. Ltd, Japan
FIND	Diagnostic	GenoType MTBDRplus®/ Line Probe Assay (1st line drugs) A DNA strip test. Allows simultaneous molecular identification of tuberculosis and the most common genetic mutations causing resistance to rifampicin and isoniazid.	TB	Endemic countries	2008	Hain Lifescience, Germany
FIND	Diagnostic	Primo Star iLED Light-emitting diode (LED) fluorescence microscopy. Improved TB case detection, durable, affordable, energy-efficient.	TB	Endemic countries	2009	Carl Zeiss MicroImaging GmbH, Germany
FIND	Diagnostic	Xpert® MTB/RIF/ Automated nucleic acid amplification test (NAAT) Self-contained and cartridge-based technological platform that integrates sputum processing, DNA extraction and amplification, TB and MDR-TB diagnosis.	TB	Endemic countries	2010	Cepheid, USA
IDRI	Diagnostic	KalazarDetect An in vitro diagnostic medical device designed for the qualitative detection of antibodies to members of L.donovani complex in	Leishmaniasis	Endemic countries	2009	InBios, International, USA

		human serum.				
iOWH	Ingredient	Semisynthetic Artemisinin prequalified by the World Health Organization (WHO), A key ingredient in first line malaria treatments	Malaria	Endemic countries	2012	Sanofi-Aventis, USA University of California, Berkeley (UCB), USA Amyris Inc., USA
iOWH	Formulation	antibiotic Paromomycin Intramuscular Injection (PMIM) Alife-saving medicine for the treatment of visceral leishmaniasis. OWH resurrected PMIM, a drug abandoned by for-profit pharmaceutical companies, and developed it into a safe, effective and low-cost treatment for Kala-Azar.	VL	South Asia, East Africa and South America	2011	Gland Pharma, India
IVI	Vaccine	Killed whole-cell oral cholera vaccine mORC-Vax™ (Vietnam), Shanchol™ (India) Reformulated a bivalent, killed whole-cell oral cholera vaccine, by replacing a high toxin-producing strain with a low toxin-producing strain and changing the antigen content of other strains.	Cholera	India, Vietnam	2011	Vabiotec, Vietnam Shantha Biotechnics, India Eubiologics, Korea
MVP	Vaccine	MenAfriVac™ Adapted existing Meningitis vaccines to make them suitable for Meningitis A	Meningitis A	Sub-Saharan Africa	2010	(PATH and WHO Partnership) Syncs Bio/Netherlands -Serum Institute of India Center for Biologics Evaluation and Research of the U.S FDA Serum Institute of India (SILL) Ltd, Pune, India UK National Institute for Biological Standards (NIBSC) Trial sites in India and Africa
CONRAD	Contraceptive	SILCS Diaphragm Safe, comfortable, and easy to use, expanding non-hormonal contraceptive options for women Launched in 6 European countries in June, 2013. Next step is regulatory submission to the United States Food and Drug Administration for market approval in the United States. PATH and research partners in Uganda, India, and South Africa also aim to introduce SILCS in low-resource settings.	Contraception /HIV	Europe	2013	Collaboration between PATH, a Seattle, Washington-based global health non-profit; CONRAD, a reproductive health product development organization operated through the Eastern Virginia Medical School in Norfolk, Virginia; the United States Agency for International Development (USAID); and other partners. In 2010, PATH licensed the SILCS design to Kessel Marketing & Vertriebs GmbH (Kessel), a private-sector company in Frankfurt, Germany.
Total no. of products: 23 (This table was last updated in January 2014)						

Chapter 2

Table 10. Disease Coverage by PDP

	AERAS	MMV	CONRAD	DVI	TB Al	HVTN	IAVI	IPM	MDP	MVI	MVP	PDVI	SAAVI	TBVI	CPDD	IVCC	FIND	IVI	OWH	Sabin PDP	IDRI	EVI	DNDi	# of PDPs covering the disease
Malaria		x								x						x	x		x		x	x	x	8
Leishmaniasis															x				x	x	x	x	x	6
Tuberculosis	x				x									x			x				x	x		6
HAT															x		x						x	3
Chagas																				x	x	x	x	4
Dengue				x								x				x						x		4
HIV			x			x	x	x	x				x									x	x	8
Helminths																			x	x			x	3
Typhoid																		x						1
Cholera/Diarrheal disease																		x	x					2
Leprosy																					x			1
Meningitis											x										x			1
Schistosomiasis																				x				1
Pneumonia/Influenza																		x			x			2
Shigellosis																								1
# of diseases covered by the PDP		1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	3	4	4	4	6	6	6	
	←																						→	
	Specialist PDP																						Generalist PDP	

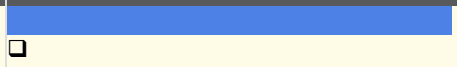
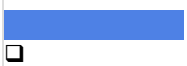
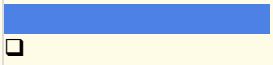
Chapter 3

Table 11. Survey questionnaire

1. Indicate the name of the PDP

Text Response
Drugs for Neglected Diseases Initiative (DNDi)
TBVI Tuberculosis Vaccine Initiative (TBVI)
Dengue Vaccine Initiative (DVI)
Global Alliance for TB Drug Development (TB Alliance)
IVCC
International Vaccine Institute (IVI)
PATH Malaria Vaccine Initiative (MVI)
Foundation for Innovative New Diagnostics (FIND)
Sabin Vaccine Institute PDP
International Partnership for Microbicides (IPM)
Medicines for Malaria Venture (MMV)
PATH/WHO Meningitis Vaccine Project (MVP)
AERAS
CONRAD
European Vaccine Initiative (EVI)
Microbicides Development Programme (MDP)

2. Indicate the name of the survey respondent and whether you authorize us to disclose the name in our research report.

#	Answer		Response	%
1	Name		15	94%
2	I authorize disclosure of my name in any EPFL research		6	38%
3	I do not authorize disclosure of my name in any EPFL research		9	56%

3. How important is IP management for the PDP?

#	Answer		Response	%
1	low		0	0%
2	medium		5	33%
3	high		10	67%
	Total		15	100%

4. Does the PDP have a defined IP management policy?

#	Answer		Response	%
1	yes		13	87%
2	No		2	13%
	Total		15	100%

5. Is the IP management policy publicly available and/or published?

#	Answer		Response	%
1	Yes		5	38%
2	No		8	62%
	Total		13	100%

6. What are the benefits of having a defined IP management policy?

Text Response
Clear guidelines internally and externally. Reference to the policy during negotiations
Clear view on the position of the PDP
There are many as have been laid out in the IP Handbook. In particular, DVI needs to assure its private sector partners that is is aware of the IP situation and will respect and promote IP protection for the benefit of the companies and for the benefit of the public sector.
To ensure that our management team, our board, donors and key strategic partners have a clear understanding of what our IP policy is.

Clarity and standardisation between partners
While it is necessary to consider each case on its own merits, a policy establishes the guidelines enabling rapid and consistent decision-making. By the way, I assume that you refer to patent filing policy when you talk about "IP management policy".
Sets scope of what is permitted and not, clear to partners how we operate
To ensure we can advance the PDP Programs without any potential or perceived barriers
MMV needs to address IP management in all of its research programmes as all programmes generate Foreground IP. Decisions need to be made on ownership of IP, protection of IP, rights to the IP, etc.
Policy is available upon request. A defined policy provides clarity for employees and guides our negotiations with other organizations with whom Aeras has collaborative relationships.
clear guidelines to execute third party agreements, eg, contracts, MTAs, sublicenses, etc., and business plans
To ensure that products will be made available to the target populations in low income settings at affordable prices
Sets out the agreed position as to how IP generated under the MDP programme will be managed.

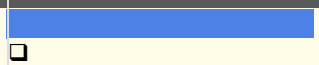
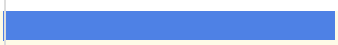
Statistic	Value
Total Responses	13

7. What are the benefits of not having a defined IP management policy?

Text Response
Flexibility

Statistic	Value
Total Responses	1

8. Do any of the following characteristics of the PDP influence the PDP approach to IP management?

#	Answer		Response	%
1	Non-profit nature		13	81%
2	Work to large extent through R&D partnerships/collaborations		12	75%
3	R&D plus access mission		14	88%
4	Any other		2	13%

Any other

❑ Our product will not command a dual market (at least not to a significant level). If it did, we would probably be diligent in attempting to establish and own a patent portfolio around it in order to use potential royalties from sales industrialized countries to achieve our Global Access objectives.
❑ Advancing products that have no commercial return

9. Is there any staff in the PDP explicitly dedicated to IP management?

❑ #	❑ Answer	❑	❑ Response	❑ %
❑ 1	❑ Yes	❑	❑ 7	❑ 44%
❑ 2	❑ No	❑	❑ 9	❑ 56%
❑	❑ Total	❑	❑ 16	❑ 100%

10. What is the internal governance structure in the PDP for decision-making on IP management?

❑ Text Response
❑ Responsibility of the Director of BD and Legal, some issues brought to the Executive committee when necessary
❑ Legal counsel
❑ Any IP agreement has to be approved by the Director General. There are no other committees or review bodies.
❑ We have established an IP committee to oversee key IP decisions and to recommend any changes to our IP strategy
❑ Portfolio manager recommends to the management team
❑ We use a Consulting firm for IP. The Dir Portfolio Management is the point of contact. Decision are taken by Dir Portfolio and CSO, submitted to Director general for approval.
❑ Any decision needed will be made by MVI's Portfolio Management Committee.
❑ Contract management function, clear donor guidelines
❑ Decisions are managed by and through an Executive Board Committee
❑
❑ Executive Team
❑ Head of Legal is responsible for IP management
❑ When an invention disclosure made by an employee it is reviewed by Head of R&D (including other relevant research team members), CEO and General Counsel and a decision is made whether or not to file a patent
❑ Initial decision by contracts and program teams. Final decision by Executive Director
❑ IP issues are regulated in the contracts signed with organisations that are supported by EVI
❑ Publication/dissemination of data and results was managed by the Programme Liaison Group (specified membership, set quorum & set majority), Responsible for overall management of MDP (including monitoring achievement of programme objectives) was the Programme Management Board (all partners, set quorum & set majority)

❑ Statistic	❑ Value

Total Responses	15

11. What are the main activities undertaken in the PDP in relation to IP management?

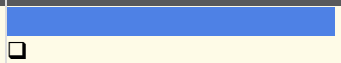
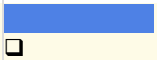
Text Response
Insuring access provisions and freedom to operate within all contracts and partnerships
In principle no IP is owned by the PDP
Mainly DVI monitors the situation. All the developers have their own IP and FTO. We do not feel the field is impeded by competing or overlapping IP claims.
Filing patents, protecting inventions, trade secrets and trademarks and licensing IP
Ensuring access through licensing if necessary.
Follow up of our patents, search for patentability by consulting firm.
Very few - we typically do not support patent filing and prosecution costs incurred by our partners.
We do not hold any IPR, its covered under our agreements with our partners
Patent protection, publications
Licensing agreements, patents
Protection of IP, in and out-licensing of IP
Review of projects, manuscripts for publications and other disclosure to ensure timely filing of patent applications.
Establishment and implementation of policy through contracts and agreements with partners. Protecting inventions by filing patents. Licensing drugs from othwer organizations.
Ensure via contractual clauses that products will be made available at affordable prices
Granting of licences/rights in respect of IP brought into/tested as part of MDP. Patentable results were not expected to be generated in the course of MDP activities.

Statistic	Value
Total Responses	15

12. Is your PDP a user of IP (has gained rights or obtained a license to use third party IP-protected products/processes/services)?

#	Answer		Response	%
1	Yes		12	75%
2	No		4	25%
	Total		16	100%

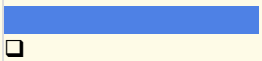
13. Does the PDP use this form of IP?

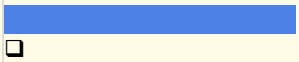
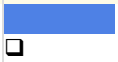
#	Answer		Response	%
1	Patents		13	87%
2	Trademarks		5	33%
3	Copyright		6	40%
4	Trade secrets		6	40%
5	Other		3	20%

Other
Technology, as in requiring agreement to technology transfer if partner is unwilling or unable to fulfill its oblgations.
Data
we only reserve IP rights in case of non-compliance with contractual obligations

Statistic	Value
Total Responses	15

14. What is the purpose of the use of patents?

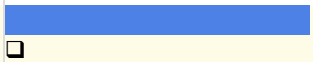
#	Answer		Response	%
1	To obtain access to a technology or knowledge that is protected by a patent		7	54%
2	To ensure freedom to operate (without infringing patents held by third parties)		7	54%

❑ 3	❑ To transfer technology to third parties		❑ 8	❑ 62%
❑ 4	❑ Any other		❑ 3	❑ 23%

❑ Any other
❑ all of the above!
❑ All of the above
❑ Comment: access to a patent never ensures freedom to operate.

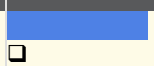
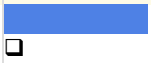
❑ Statistic	❑ Value
❑ Total Responses	❑ 13

15. How important is it for the PDP to access related know-how or capabilities of the patent holder, in addition to the right of use or license?

❑ #	❑ Answer	❑	❑ Response	❑ %
❑ 1	❑ low		❑ 0	❑ 0%
❑ 2	❑ medium		❑ 3	❑ 20%
❑ 3	❑ high		❑ 12	❑ 80%
❑	❑ Total	❑	❑ 15	❑ 100%

❑ Statistic	❑ Value
❑ Total Responses	❑ 15

16. How often does the PDP obtain a patent license that is exclusive as opposed to non-exclusive?

❑ #	❑ Answer	❑	❑ Response	❑ %
❑ 1	❑ Never		❑ 6	❑ 38%
❑ 2	❑ Rarely		❑ 6	❑ 38%
❑ 3	❑ Sometimes		❑ 2	❑ 13%
❑ 4	❑ Often		❑ 2	❑ 13%

5	All of the time		0	0%
	Total		16	100%

Statistic	Value
Total Responses	16

17. How often does the PDP obtain a patent license that is royalty-free as opposed to royalty-bearing?

#	Answer		Response	%
1	Never		4	25%
2	Rarely		1	6%
3	Sometimes		3	19%
4	Often		4	25%
5	All of the time		4	25%
	Total		16	100%

Statistic	Value
Total Responses	16

18. Does the patent status of a technology influence the PDP selection of that technology for an R&D project?

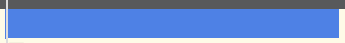
#	Answer		Response	%
1	Yes, if there is alternative technology available the PDP will choose alternative		4	27%
2	No, if good terms can be reached for the use of the patent		1	7%
3	No, if the technology is considered the best choice for		7	47%

	the project			
4	Other		3	20%
	Total		15	100%

Other
n/a
Obviously, we want to avoid royalty obligations whenever possible. As stated above, existence of a patent around a partnered technology is otherwise a minor factor contributing to our decision-making.
we only ensure that IP situation will allow making products available at affordable prices in developing countries

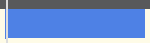
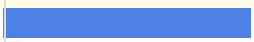
Statistic	Value
Total Responses	15

19. Is it useful for third parties to share patents with the PDP (allowing the PDP uncompensated use of a patent)?

#	Answer		Response	%
1	Yes		13	87%
2	No		2	13%
	Total		15	100%

Statistic	Value
Total Responses	15

20. Is there a particular R&D stage in which sharing of patents is more useful?

#	Answer		Response	%
1	Yes		4	36%
2	No, all are equally useful		7	64%
	Total		11	100%

Yes
Discovery
Early in development

R&D and Process development
Early development

Statistic	Value
Total Responses	11

21. Is the PDP a producer of IP (claim ownership of any form of IP)?

#	Answer		Response	%
1	Yes		11	69%
2	No		5	31%
	Total		16	100%

Statistic	Value
Total Responses	16

22. Does the PDP produce this form of IP?

#	Answer		Response	%
1	Patents		5	42%
2	Trademarks		0	0%
3	Copyright		3	25%
4	Trade Secrets		0	0%
5	Any other		4	33%
	Total		12	100%

Any other
n/a
All of the above except copyright
We rarely prosecute our "own" patents, but we do refer to MVI's Background Technology in our agreements (in effect, that would be mostly know-how and trade secret-type of IP).
data

Statistic	Value
Total Responses	12

23. Does the PDP have a policy on who may seek patents on the results of R&D projects in the PDP portfolio (i.e. whether by the PDP, individual PDP staff, the PDP with partners, or partners alone)?

#	Answer		Response	%
1	Yes		9	60%
2	No		6	40%
	Total		15	100%

Statistic	Value
Total Responses	15

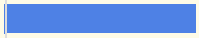
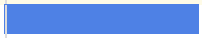
24. What is the policy on who may seek patents on the results of R&D projects in the PDP portfolio?

Text Response
We do no seek ownership of patents, we let the partner file if interested against full non-exclusive licence rights to use the patent inour activities.
The inventor applies for the patent but assigns it to IVI.
All patents are assigned to TB Alliance
Partners seek patents
Institution and joined inventors
Either the partner decides on its own (pharma company) or MMV and partners decide together. MMV may decide on its own if all the IP rights were assigned to MMV.
By PDP If solely developed by PDP employees; Jointly with collaborators if jointly developed; By collaborator if it is only developed by collaborator
owner(s) of the patentable results may seek the patents

Statistic	Value
Total Responses	8

25. For the PDP, what is the purpose of producing patents?

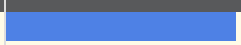
#	Answer		Response	%
1	To generate income via		2	13%

	licensing to fund activities			
2	As a defensive strategy to avoid third parties from unauthorized use of the technology or claiming ownership of patents over the technology		7	44%
3	To license patents to industry to raise their interest in partnering in manufacturing - distribution		8	50%
4	Any other		8	50%

Any other
None
n/a
Control the development and manufacturing of a compound to ensure proper use, quality and access
As stated, this is not a major driver in our strategy, as our product is not a typical dual market product.
NA
For cross licensing so that Aeras can access technology owned by others
To ensure access to products at affordable prices in the target populations
to fulfil pre-existing obligations to commercial partner & funders

Statistic	Value
Min Value	1
Max Value	4
Total Responses	16

26. Which of these situations apply to the results of R&D projects in the PDP portfolio? (in relation to who can be an assignee of the patent, not inventor)

#	Answer		Response	%
1	The PDP can hold a patent		9	60%
2	The PDP and		9	60%

	partner(s) can jointly hold a patent			
3	PDP staff or member(s) can can hold a patent in their own name		1	7%
4	A partner can hold a patent, with pre-agreed licensing terms to the PDP		10	67%
5	Any other		2	13%

Any other
n/a
A partner can hold a patent under the condition to make the products available at affordable prices in target populations

Statistic	Value
Total Responses	15

27. To what extent does the PDP share patents or is considering sharing patents (allow a third party uncompensated use)?

Text Response
If applicable, unlimited use without compensation of IP for non-profit goals
N/A
Not at all because it has no patents.
We are comfortable licensing our patents on an exclusive basis in the developed world and on a non-exclusive basis in the least developed countries
Not
Not sharing
We will consider sharing whenever it furthers achievement of our Global Access objectives.
N/A
with academic partners
it may happen (hasn't happened yet)
Have cross-licensed or shared our patents in return for global access to the final product.
Frequently
All partners have right to use for non-commercial activities

Statistic	Value
Total Responses	13

28. For the PDP, is open R&D collaboration useful (no patent claims for results of the R&D collaboration)?

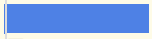
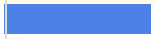
#	Answer		Response	%
1	Yes		10	67%
2	No		3	20%
3	In a particular research stage		2	13%
	Total		15	100%

In a particular research stage
Yes, when encouraging companies to work with us in identifying optimal combination drug regimens
Discovery

Statistic	Value
Total Responses	15

29. Which of the following factors influence patent licensing agreements or R&D agreements between the PDP and partners?

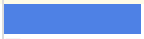
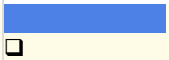
#	Answer		Response	%
1	R&D stage		12	80%
2	Target profile of the product to be developed		11	73%
3	Target price of medical product		8	53%
4	Type of partner		9	60%
5	Choice of sources to obtain the technology/knowledge/resources		7	47%
6	Specific disease that is targeted		10	67%
7	Regions / countries		9	60%

	that are targeted			
8	Markets that are targeted (private, public, purchasing entities)		7	47%
9	Source of funds of the PDP (public, philanthropic, in-dustry)		6	40%
10	Estimated cost of production		6	40%
11	Any other		2	13%

Any other
n/a
Commitment to providing access to the product to those most in need in developing countries.

Statistic	Value
Total Responses	15

30. Are pre-existing patents held by partners ever an obstacle for the successful conclusion of partnerships at any R&D stage?

#	Answer		Response	%
1	Never		3	21%
2	Rarely		5	36%
3	Sometimes		6	43%
4	Often		0	0%
5	All of the time		0	0%
	Total		14	100%

Statistic	Value
Total Responses	14

31. Are pre-existing patents held by the PDP ever an obstacle for the successful conclusion of partnerships at any R&D stage?

#	Answer		Response	%

1	Never		11	79%
2	Rarely		3	21%
3	Sometimes		0	0%
4	Often		0	0%
5	All of the Time		0	0%
	Total		14	100%

Statistic	Value
Total Responses	14

32. Are negotiations on terms for ownership of future patents ever an obstacle for the successful conclusion of partnerships at any R&D stage?

#	Answer		Response	%
1	Never		1	7%
2	Rarely		6	40%
3	Sometimes		7	47%
4	Often		1	7%
5	All of the Time		0	0%
	Total		15	100%

Statistic	Value
Total Responses	15

33. Has the PDPs done any opposition/invalidity of any IP held by third party?

#	Answer		Response	%
1	Yes		0	0%
2	No		16	100%

	Total		16	100%

Statistic	Value
Total Responses	16

34. Can you describe a case/cases?

Text Response

Statistic	Value
Total Responses	0

35. Has the PDP had any case of patent litigation/infringement to deal with?

#	Answer		Response	%
1	Yes		3	19%
2	No		13	81%
	Total		16	100%

Statistic	Value
Total Responses	16

36. Can you describe a case/cases?

Text Response
Never any litigation/nfringement issues
We have been cautious about proceeding with a particular compound held by a biotech company because of the patents surrounding that compound and our inability to obtain a license to that compound
We had dealings with an R&D partner which was in patent litigation with a third party (I am not sure if this was your question).
n/a

Statistic	Value
Total Responses	4

37. Can you share any case studies, best practice or examples of IP management / licensing deals by the PDP?

Text Response
We are currently in discussions regarding the licensing of a Phase 3-ready regimen to a global partner where we are offering a non-exclusive license to all countries of the world except the High Income Countries where we are offering an exclusive license. Our partner will pay us royalties on sales where they have an exclusive license.
Licensing deals: it is good to "stage" your agreements according to the stage of the project. E.g., if you fund an early-stage feasibility study where you are mostly interested in the resulting data, it doesn't make any sense to negotiate complete terms relating to, say, the commercialization of a product resulting from the use of the technology applied in the study.
IPM has several non-exclusive licenses for ARV technologies
n/a

Statistic	Value
Total Responses	4

References

Årdal, C. Røttingen, J.A. (2012) 'Open Source Drug Discovery in Practice: A Case Study', PLoS Neglected Tropical Diseases, 6/9: e1827.

Arrow, KJ. (1963), 'Uncertainty and the welfare economics of medical care', The American Economic Review, 53: 941-73.

Banerji B., Pecault B. (2007) Pragmatic and Principled: DNDi's approach to IP Management, in Krattiger A., Mahoney R.T., Nelsen L., Thomson JA, Bennett AB, Satyanarayana K, Graff GD, Fernandez C, and Kowalski SP, eds. *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*. MIHR: Oxford, U.K., and PIPRA: Davis, California, U.S.A.

Belderbos R., Cassiman B., Faems D., Leten B., Van Looy B. (2014) 'Co-ownership of intellectual property: Exploring the value-appropriation and value-creation implications of co-patenting with different partners', Research Policy 43, 841–852.

Bessen, J., Meurer, M. (2008) *Patent Failure. How Judges, Bureaucrats, and Lawyer's put Innovation at Risk*. Princeton University Press, Princeton.

Bio Ventures for Global Health (2012) *Developing New Drugs and Vaccines for Neglected Diseases of the Poor: The Product Developer Landscape.* San Francisco: Bio Ventures for Global Health.

Brooks, A.D. Wells, W.A. McLean, T.D. Khanna, W.A. et al (2010) 'Ensuring that Developing Countries have Access to New Healthcare Products: The Role of Product Development Partnerships', Innovation Strategy Today, 3:1-5.

Cernuschi, T. Furrer, E. Schwalbe, N. Jones, A. et al (2011) 'Advance Market Commitment for Pneumococcal Vaccines: Putting Theory into Practice', Bulletin of the World Health Organization, 89: 913-18.

Chataway, J. Brusoni, S., Cacciatori, E. Hanin, R. et al (2007) 'The International AIDS Vaccine Initiative (IAVI) in a Changing Landscape of Vaccine Development: A Public Private P artnership as Knowledge Broker and Integrator', European Journal of Development Research, 19/1: 100-17.

Chataway, J. Hanlin, R. Mugwagwa, J. Muraguri, J. (2010) 'Global Health Social T echnologies: Reflections on Evolving Theories and Landscapes', Research Policy, 39: 1277-88.

Cameron A., Ewen M., Ross-Degnan D., Ball D., Laing D. (2009) 'Medicine Prices, Availability, and Affordability in 36 Developing and Middle-Income Countries: A Secondary Analysis', The Lancet, 373:9659, 240 – 249.

Clark K., Cavicchi J., Jensen K., Fitzgerald R., Bennett A., Kowalski S.P. (2001) 'Patent data mining: A tool for accelerating HIV vaccine innovation', Vaccine, 29, 4086–4093.

Coase, R. (1937), 'The Nature of the Firm', Economica, 4:16, 386:405.

Coase, R. (1960), 'The Problem of Social Cost', Journal of Law & Economics, 3:1.

Cockburn I. (2005) 'Blurred Boundaries: Tensions Between Open Scientific Resources and Commercial Exploitation of Knowledge in Biomedical Research'. Prepared for the Advancing Knowledge and the Knowledge Economy Conference, January 10-11, 2005, National Academy of Sciences, Washington, DC.

Cockburn, I. (2006) 'Is the Pharmaceutical Industry in a Productivity Crisis?', Innovation Policy and the Economy, 7.

Cockburn, I. Henderson R. (2001) 'Scale and Scope in Drug Development: Unpacking the Advantages of Size in Pharmaceutical Research', Journal of Health Economics, 20: 1033–1057.

Cohen, W.M., (2010) 'Fifty years of empirical studies of innovative activity and performance', in Hall B., Rosenberg H., eds. Handbook of The Economics of Innovation, 1, 129 – 213.

Cohen, W.M., Nelson, R.R., Walsh, J.P., (2000) Protecting their intellectual assets: appropriability conditions and why U.S. manufacturing firms patent (or not). National Bureau of Economic Research Working Study 7552.

Comanor W., Scherer P.M, (2013) Mergers and Innovation in the Pharmaceutical Industry. Journal of Health Economics, 32, 106 – 113.

CSDH (2008), *Closing the gap in a generation: health equity through action on the social determinants of health*, Final Report of the Commission on Social Determinants of Health. Geneva, World Health Organization.

David P., Hall B., Toole A., (1999) 'Is public R&D complement or substitute for private R&D? A review of econometric evidence', NBER Working Study No. 7373.

DNDi, MSF (2012) *Medical Innovation for Neglected Patients* (Geneva, 2012; pubd online 2012) http://www.msfaccess.org/sites/default/files/MSF_assets/Innovation/Docs/MedInno_Report_MedInnforNegPatients_ENG_2012.pdf> accessed 24 June 2013.

DiMasi, J. Hansen, R. Grabowski, H. (2003) 'The Price of Innovation: New Estimates of Drug Development Costs', Journal of Health Economics, 22: 151-85.

Eiss R., Hanna KE., Mahoney RT., (2007) Ensuring Global Access through Effective IP Management: Strategies of Product-Development Partnerships, in Krattiger A., Mahoney R.T., Nelsen L., Thomson JA, Bennett AB, Satyanarayana K, Graff GD, Fernandez C, and Kowalski SP, eds. *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*. MIHR: Oxford, U.K., and PIPRA: Davis, California, U.S.A.

Ekins, S. Waller, C. Bradley, M. Clark, A. Williams, A. (2013) 'Four Disruptive Strategies for Removing Drug Discovery Bottlenecks'. Drug Discovery Today. 18:5/

European Commission (2009) Competition DG. Pharmaceutical Sector Inquiry: Final Report. Adoption Date: 8 July 2009.

Frenk, J. Moon, S. (2013), 'Governance Challenges in Global Health', The New England Journal of Medicine, 68, 936-42.

Galea G., Mckee M. (2014) 'Public-private partnerships with large corporations: setting the ground rules for better health,' Health Policy, 115, 138 – 140.

Gallini N., Scotchmer S. (2002) 'Intellectual Property: When Is It the Best Incentive System?' NBER Chapters, in Jaffe A., Lerner J., Stern S., eds. *Innovation Policy and the Economy, Volume 2, National Bureau of Economic Research*, MIT Press, 51-78.

Geuna, A. and Rossi, F. (2011) 'Changes to university IPR regulations in Europe and the impact on academic patenting,' Research Policy 40:8, 1068-1076.

Global Health Technologies Coalition, (2013) *Financing and Coordination of Health Research: Perspectives from Nonprofits on Accelerating Product Development and Improving Access for Low- and Middle-Income Countries*. Vol. 2. Washington, DC.

Grace C. (2006) *Developing New Technologies to Address Neglected D iseases: The Role of Product Development Partnerships and Advanced Market Commitments*, London: DFID Health Resource Centre.

Grace C. (2010) *Product Development Partnerships (PDPs): Lessons from PDPs Established to Develop New Health T echnologies for Neglected D iseases*, London: DFID Human Development Resource Centre.

Guedj, Scharfstein (2004) Organizational Scope and Investment: Evidence from the Drug Development Strategies and Performance of Biopharmaceutical Firms, NBER Working Papers 10933, National Bureau of Economic Research.

Hagerdoorn J., (2002) 'Inter-firm partnerships: an overview of major trends and patterns since 1960,' Research Policy, 31:4, 477 - 492.

Hall B., Ziedonis R. (2001) 'The patent paradox revisited: an empirical study of patenting in the U.S. semiconductor industry 1979-1995', RAND Journal of Economics, 32:1, 101- 128.

Hall, B. Lerner, J. (2010) 'The Financing of R&D and Innovation', in Hall B., Rosenberg, N. (eds), Handbook of the Economics of Innovation. Vol., 1,: 609-93, Elsevier..

Hanel P. (2006) 'Intellectual property rights business management practices: A survey of the literature', Technovation, 26:8, 95–931.

Henderson R., Cockburn I. (1996) 'Scale, Scope, and Spillovers: The Determinants of Research Productivity in Drug Discovery', The Rand Journal of Economics, 27/1: 32-59.

Hemphill C. S., Sampat N. B. (2012) 'Evergreening, patent challenges, and effective market life in pharmaceuticals,' Journal of Health Economics, 31: 2, 327-339.

Hertzfeld R. Henry, Albert, Vonortas S. Nicholas, (2006) 'Intellectual property protection mechanisms in research partnerships', Research Policy, 35, 825–838.

Hobday, M. Davies, A. Prencipe, A. (2005) 'Systems Integration: A Core C apability of the Modern C orporation', Industrial and Corporate Change, 14/6: 1109-143.

Hoen E., Berger J., Calmy A., Moon S., (2011) 'Driving a decade of change: HIV/AIDS, patents and access to medicines for all', Journal of the International AIDS Society, 14:15.

IFPMA (2012) *Status Report on Pharmaceutical R&D to Address Diseases that Disproportionately Affect People in Low and Middle Income Developing C ountries* (Geneva, 2012; pubd online 2012) <http://www.ifpma.org/fileadmin/content/Publication/2013/IFPMA_R_D_Status_Report_Neglected_Conditions.pdf> accessed 24 June 2013.

Juliano, R.L (2013) 'Pharmaceutical Innovation and Public Policy: The Case for a New Strategy for Drug Discovery and Development', Science and Public Policy, 40: 393-405.

Kapczynski A. Chaifetz S., Katz Z., Benkler Y., (2005) 'Addressing Global Health Inequities: An Open Licensing Approach for University Innovations', Berkeley Tech L.J. 20, 1031-1113.

Krattiger A., (2007) Freedom to Operate, Public Sector Research, and Product-Development Partnerships: Strategies and Risk-Management Option, in Krattiger A., Mahoney R.T., Nelsen L., Thomson JA, Bennett AB, Satyanarayana K, Graff GD, Fernandez C, and Kowalski SP, eds. *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*. MIHR: Oxford, U.K., and PIPRA: Davis, California, U.S.A.

Krattiger A., Mahoney R.T., Chiluwal A. and Kowalski S.P. (2012) Global Challenges Report: Patent Information, Freedom to Operate and "Global Access": A Case Study of Dengue Vaccines under Development, WIPO, Geneva.

Koplan, J., Bond, T., Merson, M., Reddy, K., Rodriguez, M., Sewankambo, N., Wasserheit, J. (2009), 'Towards a Common Definition of Global Health', The Lancet, 373:9679, 1993–1995.

Kremer, M. (2001) 'Creating Markets for New Vaccines-Part I: Rationale'. In: Jaffe, A. Lerner, J. Stern, S. (eds.) *Innovation Policy and the Economy*, pp. 35-72. Cambridge, MA: MIT Press.

Lerner J., (2009) 'The empirical impact of intellectual property rights on innovation: puzzles and clues', American Economic Review: Papers and Proceedings, 99:2.

Levin R.C., Klevorick, A.K., Nelson, R.R., Winter, S.G. (1987) Appropriating the returns from industrial research and development. Brookings Papers on Economic Activity, 18:3, 783–820.

Levin R.C. (1988) 'Appropriability, R&D Spending, and Technological Performance', The American Economic Review, 78:2, 424-428.

Levine, R. Kremer, M. Albright, A. (2005) *Making Markets for Vaccines: Ideas to Action. Report of the Center for Global Development Advance Market Commitment Working Group.* Washington D.C: Center for Global Development.

Light, D. Warburton, R. (2011) 'Demythologizing the High Costs of Pharmaceutical Research', BioSocieties, 6: 34–50.

Light, D. Lexchin, J. (2012) 'Pharmaceutical Research and Development: What Do We G et for All That Money?,' BMJ, 345:e4348.

Metcalfe J.S, Ramlogan R. (2008) 'Knowledge, Understanding and the Dynamics of Medical I nnovation,' MPRA Paper, 9112, University Library of Much, Germany.

Mahoney R.T, Krattiger A., Clemens J., Curtiss R. (2007) 'The introduction of new vaccines into developing countries', Global Access Strategies. 25, 4003–4011.

Matter A., Keller T. (2008) 'Impact of non-profit organizations on drug discovery: opportunities, gaps and solutions', Drug Discovery Today, 13;7/8.

Mazzoleni R., Nelson R. (1998) 'The benefits and costs of strong patent protection: a contribution to the current debate', Research Policy, 27:3, 273-284.

Maurer SM., Rai A., Sali A. (2004) 'Finding Cures for Tropical Diseases: Is Open Source an Answer?' PLoS Med 1(3): e56.

Médecins Sans Frontières (2001) *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases* (Geneva; pubd online September 2001)<http://www.doctorswithoutborders.org/publications/reports/2001/fatal_imbalance_short.pdf> Accessed 24 October 2012.

Médecins Sans Frontières (2013) *Global Vaccines Community Must Bring P rice of New Vaccines down* (Geneva; pubd online April 2013) **<**http://www.msfaccess.org/our-work/vaccines/article/2040> accessed 5 July 2013.

Menell P., Scotchmer S. (2007) Intellectual Property Law, in Polinsky M., Shavell S. (eds) *Handbook in Law and Economics*, Volume 2, North - Holland, Oxford, UK. 1473 – 1557.

Moran, M. (2005) 'A Breakthrough in R&D for Neglected Diseases: New W ays to Get the Drugs We N eed', PLoS Medicine, 2/9: e302.

Moran, Mary (2005) *The New Landscape of Neglected Disease Drug Development*, London: LSE and Wellcome Trust.

Moran M., Ropars AL., Guzman J., Diaz J., Garrison C. (2005) *The new landscape of neglected disease drug development*, London School of Economics and Political Science and the Wellcome Trust, London.

Moran M., Guzman J., Ropars AL., Illmer A. (2010) 'The role of Product Development Partnerships in research and development for neglected diseases', International Health, 2:2, 114 – 122. doi:10.1016/j.inhe.2010.04.002

Moran, M. Guzman, J. Ropars, A.L. Illmer, A. (2010) 'The Role of Product Development P artnership in Research and Development for Neglected D iseases', International Health, 2/2: 114-122.

Morel, C. Acharya, T. Broun, D. Dangi, A. Elias, C. Ganguly, N.K. Gardner, C. Gupta, R.K. Haycock, J. Heher, A. Hotez, P. Kettler, H. Keusch, G. Krattiger, A. Kreutz, F. Lall, S. Lee, K. Mahoney, R. Martinez-Palomo, A. Mashelkar, R.A. Matlin, S. Mzimba, M. Oehler, J. Ridley, R. Senanayake, P. Singer, P. Yun, M. (2005) 'Health Innovation Networks to Help Developing Countries Address Neglected Diseases', Science, 309.

Morgan, S. Grootendorst, P. Lexchin, J. Cunningham et al (2011) 'The Cost of Drug D evelopment: A Systematic Review', Health Policy, 100/1: 4-17.

Mowery D., Sampath B. (2014) Universities in National Innovation Systems, on Fagerberg J., Mowery D., Nelson R., (eds) *Handbook of Innovation*, Oxford University Press.

Mueller E., Cockburn I., Magarvie M. (2013) 'Access to Intellectual Property for Innovation: Evidence on problems and coping strategies from German firms', Research Policy, 42:2, 529-541.

Munos, B. (2005) 'Lessons from 60 Years of Drug Discovery', Nature Reviews Drug Discovery, 8/12: 959-968.

Muñoz-Tellez, V., Visentin, F., Foray, D., Gaule, P. (2014) 'Can medical products be developed on a not-for-profit basis? The case of Product Development Partnerships', Science and Public Policy, doi: 10.1093/scipol/scu049.

MVI, GSK (2013) *Fact Sheet: The RTS,S Malaria Vaccine Candidate* (Geneva; pubd October 2013) <http://www.malariavaccine.org> accessed 25 October 2013.

Nelson, R. and Winter, S. (1982), *An Evolutionary Theory of Economic Change*. Cambridge, Massachusetts: The Belknap Press of Harvard University Press.

Nelson R. (2009), 'Building effective 'innovation systems' versus dealing with 'market failures' as ways of thinking about technology policy', in Foray, D. (ed.), *The New Economics of Technology Policy*.

Ostrom, E. (2009), *Beyond Markets and States: Polycentric Governance of Complex Economic Systems*, Nobel Prize Lecture.

Papaioannou, T. Wield, D. Chataway, J. (2008) 'Knowledge Ecologies and Ecosystems? An Empirically Grounded R eflection on Recent Developments in Innovation Systems Theory', Environment and Planning C: Government and Policy, 27/2: 319 – 339.

Paul, S. Mytelka, D. Dunwiddie, C. Persinger, C. et al (2010) 'How to Improve R&D Productivity: The Pharmaceutical Industry's Grand C hallenge', Nature Reviews Drug Discovery, 3/9: 203-14.

Pedrique B., Strub-Wourgaft N., Some C., Olliaro P., Trouiller P., Ford N., Pécoul B., Bradol J, (2013) 'The drug and vaccine landscape for neglected diseases (2000 – 2011): a systemic assessment', Lancet Global Health, 1, 371 – 379.

Policy Cures (2012) *G-FINDER: Global Funding of Innovation for Neglected Diseases, Report for 2012*, Australia and UK: Policy Cures.

Ridley, R. (2001) 'Putting the Partnership into Public Private Partnerships', Bulletin of the World Health Organization, 79/8: 694-97.

Ridley, R. (2004) 'Product Development Public Private Partnerships for Diseases of Poverty: Are There More Efficient Alternatives? Are There Limitations?', IPPPH Meeting, London, April 15 and 16, 2004.

Rockett K., (2010) Property Rights and Invention, Chapter 7, in Hall B., Rosenberg H., eds. Handbook of The Economics of Innovation, 1, 315 – 380.

Roijjakers N. and Hagedoorn J., (2006) 'Inter-firm R&D partnering in pharmaceutical biotechnology since 1975: Trends, patterns, and networks', Research Policy, 35:3, 431– 446.

Rosenberg, N. (2009), 'Some Critical episodes in the progress of medical innovation: An Anglo-American Perspective', Research Policy, 38:2, 234:242.

Røttingen, J.A. Regmi, S. Eide, M. Young, A. et al (2013) 'Mapping of Available Health Research and Development Data: What's There, What's Missing, and What Role Is There for a Global Observatory?', The Lancet, 382/9900: 1286–307.

Sampat B., (2009) The dismal science, the crown jewel and the endless frontier, in Foray D., ed. *The new economics of technology policy*, Edward Elgar, 148 – 162.

Sampat, B. Lichtenberg, F. (2011) 'What Are The Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation?' Health Affairs, 30/2: 332-39.

Scotchmer S., (1998) 'R&D Joint Ventures and other Cooperative Arrangements,' In Anderson R. and Gallini N., eds. *Competition Policy and Intellectual Property Rights in the Knowledge-Based Economy*, Industry Canada Research Series. University of Calgary Press.

Scotchmer S., (2003) 'Intellectual Property--When is it the Best Incentive Mechanism for S&T Data?' (testimony), in Esanu, J.M. and Uhlir, P.F., eds. The Role of Scientific and Technical Data and Information in the Public Domain: Proceedings of a Symposium, pp. 15-18. Washington,D.C.: National Academies Press.

Sen A. (1993), Capability and well-being. In Nussbaum, MC (ed.), *The Quality of Life*, Clarendon Press: Oxford.

Sen, A. (2002), 'Why health equity?' Health Economics, 11:8, 659 – 666

Shapiro C., (2001) Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting, in Jaffe A., Lerner J., Stern J, eds. *Innovation policy and the economy*, National Bureau of Economic Research, MIT Press, 1, 119-150.

Sherry F., Teece J., (2004) 'Royalties, evolving patent rights, and the value of innovation', Research Policy, 33:2, 179-191.

Schuhmacher, A. Germann, P. Trill, H. Gassmann, O. (2013) 'Models for Open Iopen nnovation in the Pharmaceutical Industry'pharmaceutical industry, Drug Discovery Today, 18: 23–24.

Scudellari, M. (2011) 'Are Advance Market C ommitments for Drugs a Real Advance?', Nature Medicine, 17/2: 139-39.

So, A. Ruiz-Esparza, Q. (2012) 'Technology Innovation for Infectious Diseases in the Developing W orld', Infectious Diseases of Poverty, 1: 2.

Sridhar, D. (2012) 'Who Sets the Global Health Research Agenda? The Challenge of Multi-BiFinancing', PLoS Med, 9/9. e1001312.

Sternitzke C., (2013) 'An exploratory analysis of patent fencing in pharmaceuticals: The case of PDE5 inhibitors', Research Policy, 42:2, 542-551

Taubman A., (2010) 'A typology of intellectual property management for public health innovation and access: design considerations for policy makers', Open AIDS Journal, 4, 4 – 24.

Teece. D. (2012) 'Dynamic Capabilities: Routines versus Entrepreneurial Action,' Journal of Management Studies, 29/8.

The Boston Consulting Group (2010), *Path Vaccine Product Development Assessment: Summary of Findings*, (Boston; pubd July 2010) <http://www.path.org/files/OTP-bcg-vacc-dev-eval.pdf> accessed 14 May 2013.

Trouiller, P. Olliaro, P. Torreele, E. Orbinski, J. et al (2002) 'Drug Development for Neglected Diseases: A Deficient Market and a Public Health Policy Failure', The Lancet, 359: 2188–94.

Toole, A. (2012) 'The Impact of Public Basic Research on Industrial Innovation: Evidence from the Pharmaceutical Industry', Research Policy, 41: 1-12.

UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (2007) *Making a Difference: 30 Years of Research and Capacity Building in Tropical Diseases*. Geneva: World Health Organization.

UN Office of the High Commissioner for Human Rights (OHCHR), Fact Sheet No. 31, The Right to Health, June 2008, No. 31, available at: http://www.refworld.org/docid/48625a742.html (accessed 22 September 2014).

Webber, D. Kremer, M. (2001) 'Perspectives on Stimulating Industrial R esearch and Development for Neglected Infectious Diseases', Bulletin of the World Health Organization, 79: 735–41.

Wells, S. Diap, G. Kiechel, J. (2013) 'The Story of Artesunate–Mefloquine (ASMQ), Innovative Partnerships in Drug Development: Case Study', Malaria Journal, 12:68.

Williamson, O. (2000) The New Institutional Economics: Taking Stock, Looking Ahead, *Journal of Economic Literature*, 37: 595–613.

Winter G.S. (2006) The logic of appropriability: From Schumpeter to Arrow to Teece. Special issue commemorating the 20th Anniversary of David Teece's article, "Profiting from Innovation", in Research Policy, 35:8, Pgs. 1100–1106.

World Health Organization (2006) *Public Health-Innovation and Intellectual Property Rights: Report of the Commission on Intellectual Property Rights, Innovation and Public Health*. Geneva: World Health Organization.

World Health Organization (2010) *First WHO Report on Neglected Tropical Diseases: Working to Overcome the Global Impact of Neglected Tropical Diseases*. Geneva: World Health Organization.

World Health Organization (2012a) The Evolving Threat of Microbial Resistance, Options for Action. World Health Organization, Geneva.

World Health Organization (2012b) *Research and Development to Meet Health Needs in Developing Countries: Strengthening global Financing and Coordination. Report of the Consultative Expert Working Group on Research and Development: Finance and Coordination.* (Geneva; pubd April 2012) <http://www.who.int/phi/CEWG_Report_5_April_2012.pdf> accessed 3 July 2013.

Velasquez G. (2014) Public private partnerships in global health: putting business before health? South Centre Research Study 49, South Centre, Geneva

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  Ecole Polytechnique Federale de Lausanne
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- Coordinator, Innovation and Access to Knowledge Programme — 2014
  South Centre
  Geneva, Switzerland

- Manager, Innovation and Access to Knowledge Programme — 2010 - 2014
  South Centre
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- Programme Officer, Innovation and Access to Knowledge Programme — 2006 - 2010
  South Centre
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- Research Assistant — 2005 - 2006
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  Prof. Duncan Matthews
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Education

- American High School 1997
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- BA in International Relations 2002
  El Rosario University
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- MSc Development Management 2004
  Department of Economics
  London School of Economics
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Technical Skills

All Microsoft packages; SAP Finance and HR Modules; Website development: Dreamweaver 7.0;

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Awards

Alban Scholar, European Commission 2003 – 2004

Awarded one of 250 scholarships among over 6500 Latin American postgraduate and doctoral candidates

President, Colombian Society, London School of Economics 2003 - 2004

Selected Publications

- Muñoz-Tellez, V., Visentin, F., Foray, D., Gaule, P. (2014) 'Can medical products be developed on a not-for-profit basis? The case of Product Development Partnerships', Science and Public Policy, doi: 10.1093/scipol/scu049.

- Muñoz-Tellez, V., Zografos, D. (2014) Traditional Knowledge as a source for innovation, in Gervais, D. (ed), Intellectual Property, Trade and Development, Oxford University Press.

- Muñoz-Tellez, V. (2010) Dispute Settlement Under the TRIPS Agreement: The United States–Brazil (2000) and United States–Argentina Patent Disputes, In *Research Handbook On The Interpretation And Enforcement Of Intellectual Property Under WTO Rules*, (Correa. C. Ed.), Edward Elgar Publishing, UK.

- Muñoz-Tellez, V., Musungu, S. (2010) Access to Knowledge at WIPO: the development agenda and the debate on the proposed broadcasting treaty. In Access to knowledge in the age of intellectual property. G. Krikorian. A. Kapczynski. Eds. New York: Zone Books; Cambridge, Mass. USA.

- Muñoz-Tellez, V. (2009) The Changing Global Governance of Intellectual Property Enforcement: A New Challenge for Developing Countries. In IP Enforcement: International Perspectives, Li X, Correa M. C. (Eds), Edward Elgar Publishing, UK. 2009.

- Muñoz-Tellez, V., Biadgleng, E. (2008) The Changing Structure and Governance of Intellectual Property Enforcement, Research Paper 15, South Centre, Geneva.

- Muñoz-Tellez, V., Biadgleng, E., Asfaha, S. (2007) South-South Cooperation for Industrial Development, Report commissioned by UNIDO, Vienna.

- Matthews, D., Muñoz-Tellez, V. (2008) Intellectual Property Rights and Multilateral Institutions, in Desai Vandana, Potter Robert B. (Eds.), Companion to Development Studies, Oxford University Press, USA; 2 edition.

- Matthews, D., Muñoz-Tellez, V. (2007) Parallel Trade: A Users Guide, in (eds. Krattiger, Mahoney, Neilsen et al.) Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices, MIHR: Oxford, UK.

- Muñoz-Tellez, V., Waitara, C. (2007) An Analysis of the Impact of the Treaty on the Protection of Broadcasting Organizations and Cablecasting Organizations on Developing Countries, Research Paper 9, South Centre.

- Muñoz-Tellez, V., Matthews, D. (2006) 'Bilateral technical assistance and the TRIPS agreement: the United States, Japan and the European Communities in comparative perspective', *Journal of World Intellectual Property*, 9:6, 629-653.

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