Chapter 4: Report of the final project workshop

SOUTH CENTRE

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

The South Centre and the Ecole Polytechnique Federale de Lausanne, with the support of the Swiss Network for International Studies, invite you to a

Workshop on the economics of innovation of product development partnerships (PDPs) for neglected diseases

3 April 2014

Venue: South Centre, 17-19 Chemin du Champ d'Anier, 1208, Geneva

9 :00 – 9 :30	Welcome and registration	
9 :30 – 10 :00	*Session 1 : study presentations* Public-private partnerships in global health	German Velasquez, Special Advisor on Health and Development, South Centre
10 :00 –10 :45	Can medical products be developed on a non- profit basis ? Exploring PDPs for neglected diseases	Viviana Munoz, Manager IAKP, South Centre, and PHD researcher, EPFL
10 :45 –11 :00	*Coffee break*	
11 :00 –12 :00 12:00 – 13:00	*Session 2: interactive panel* What is the future of product development partnerships? Questions and answers	Chair: Dominique Foray, Chair of Economics and Management of Innovation, EPFL Patrick Gaule, Assistant Professor at CERGE, Czech Republic Paul Herrling, Chair, Novartis Institute for Tropical Diseases Jean François Alesandrini, Director of Policy and Fundraising, DNDi Keith Neroutsos, Director of Procurement, and Steve Brooke, Advisor, Commercialization, PATH Carlos Correa, Special Advisor on IP and Trade, South Centre
13:00-14:00	Lunch – South Centre	

Workshop report

I. Session 1: Presentations

In this session, two presentations were made, concerning three papers that were developed as part of the project.

I.1 German Velasquez presented a paper titled "Public-private partnerships in Global Health: putting business before health?" He started his presentation by stating the main conclusions of his work: (i) there is scarce knowledge about Public Private Partnerships (PPPs) and in particular Private Development Partnerships (PPPs); (ii) PDPs are a new experiment and it is not appropriate to say that they are a model; (iii) there is the need to bring in PDPs within government oversight. All the PDPs are outside WHO and, if WHO is recognized as the global coordinator in term of health issues, this might represent a problem.

Velasquez illustrated the PPPs and PDPs background in the United Nations (UN) context. PPPs started at the end of the 1990s with the reform of the UN system promoted by Kofi Annan. "In response to the Resolution 55/125 the UN General Assembly asked the Secretary General "to seek the views of all Members States on ways and means to enhance cooperation between the United Nations and all relevant partners, in particular the private sector, on how to enhance cooperation with the United Nations" (Velasquez, 2014, pp. 1). On the other side, the precursor of PDPs can be associated with the Special Programme for Research and Training in Tropical Diseases (TDR) created by WHO. Velasquez stressed the lack of convergence towards a single agreed-upon definition of PPPs within the UN system and the existence of some paradox in how the health public issues are managed. For instance, he expresses the concern that WHO – as one of the UN agencies with the largest number of PPPs - is not part of the UN National Global Compact, an initiative promoted by the UN to encourage business worldwide to align their activities with universally accepted principles in the areas of human rights, labor, environment and anti-corruption. One of the paradoxes is also that in the 10 core principles stated by the UN Global Compact there are no references to Public Health or to the right to access to health care.

The PDPs are defined as "one variant of the public private partnerships focused on improving health in developing countries. PDPs are focused on product discovery and development, as opposed to partnerships focused exclusively on delivery of existing technologies (so called ''access partnerships'') or health service delivery" (Velasquez, 2014, pp.8).

Some figures were reported. Investment in R&D for neglected diseases covers 31 neglected diseases and 134 product areas for these neglected diseases.

According to his study, the main concerns related to PDPs activity are the following ones:

- Most of the products so far developed are incremental innovations;
- Their capacity is quite modest;
- Their activity is 100 percent sustained by donations;
- The treatment given to intellectual property is not clear;
- The 'not for profit' character of PDPs is not completely clear.

The main conclusion of his study is that there is a "need to put a global moratorium on the creation of new PPPs and PDPs until WHO is able to use its authority to set clear rules and principles for the creation of new partnerships on global health" (Velasquez, 2014, pp. 18).

1.2 Viviana Munoz presented two papers titled "Can medical products be developed on a non-profit basis? Exploring Product Development Partnerships for Neglected Diseases" and "Intellectual Property Management in Collaborative R&D: Non-Profit Medical Product Development Partnerships", respectively. The first one is currently conditional accepted at *Science and Public Policy,* the second one is under preparation for journal submission. Both papers are part of Munoz's PhD dissertation. The two papers are available upon request at viviana.munoz@epfl.ch.

The paper ''Can medical products be developed on a non-profit basis?" provides a comprehensive analysis of the role of PDPs in the landscape for the creation of new medicines for neglected disease by mapping *all* the existing PDPs, and critically illustrating how they operate. The paper "Intellectual Property Management in Collaborative R&D" focuses on a crucial aspect of the PDPs activity, the management of intellectual property rights.

The "neglected disease" expression points out a problem of insufficient new medical products developed to address diseases that have a large burden in developing countries but no or little burden in the developed world. There is no single definition of "neglected disease" and for the purpose of the study the WHO listed diseases were considered (WHO 2010) with the inclusion of three communicable diseases: tuberculosis, malaria and HIV/AIDS. The pharmaceutical industry historically has invested very little in R&D for new medical products in the area of neglected diseases. The underinvestment is due to several reasons: R&D activity is costly and risky, commercial markets are small and the individual purchasing power is limited, even though the number of patients may be very large.

A range of economic instruments have been proposed 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 the more broadly used by policy-makers. Pull mechanisms, on the other hand, such as milestone or end prizes, secured quantities or price, aim to increase market attractiveness by lowering risk of R&D and assuring revenue for the outputs.

Meanwhile, a rising number of self-governing private non-profit organizations have emerged to catalyze R&D for neglected diseases. PDPs are self-governing, private, non-profit organizations that aim to develop new medical products in the area of neglected diseases. They do so by leveraging sources of knowledge, capabilities and assets of external public, philanthropic and private sector organizations. Since the 1990s the number of PDPs has grown from one to at least 23 PDPs that have been identified in the study: AERAS, Contraceptive Research and Development (CONRAD), Consortium for Parasitic Drug Development (CPDD), Dengue Vaccine Initiative (DVI), Drugs for Neglected Diseases (DNDi), European Vaccine Initiative (EVI), Foundation for Innovative New Diagnostics (FIND), Global Alliance for TB Drug Development (TB Alliance), HIV Vaccines Trials Network (HVTN), Infectious Disease Research Institute (IDRI), Innovative Vector Control Consortium (IVCC), International AIDS Vaccine Initiative (IAVI), International Partnership for Microbicides (IPM), International Vaccine Institute (IVI), Medicine for Malaria Venture (MMV), Microbicides Development Programme (MDP), One World Heath (IOWH), Malaria Vaccine Initiative (MVI), Meningitis Vaccine Project (MVP), Pediatric Dengue Vaccines

Initiative (PDVI), Sabin PDP, South African AIDS Vaccine Initiative (SAAVI), and Turberculosis Vaccine Initiative (TVI). To date we have interviewed several representatives from four PDPs, two producing drugs (DNDI, MMV), one producing vaccines (MVP) and one producing diagnostics (FIND). An open question is still if PDPs can be defined as a model. As reported in Table 1, there are important variances among PDPs, however PDPs share common characteristics.

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
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 driven by medical needs: products developed need to be affordable and adequate to the local context to facilitate uptake. Define 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 (i.e. priority setting, governance and sources of financing)	Strategic choices: IP policy, partners 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 diversity of partners from the public and private sector. 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	

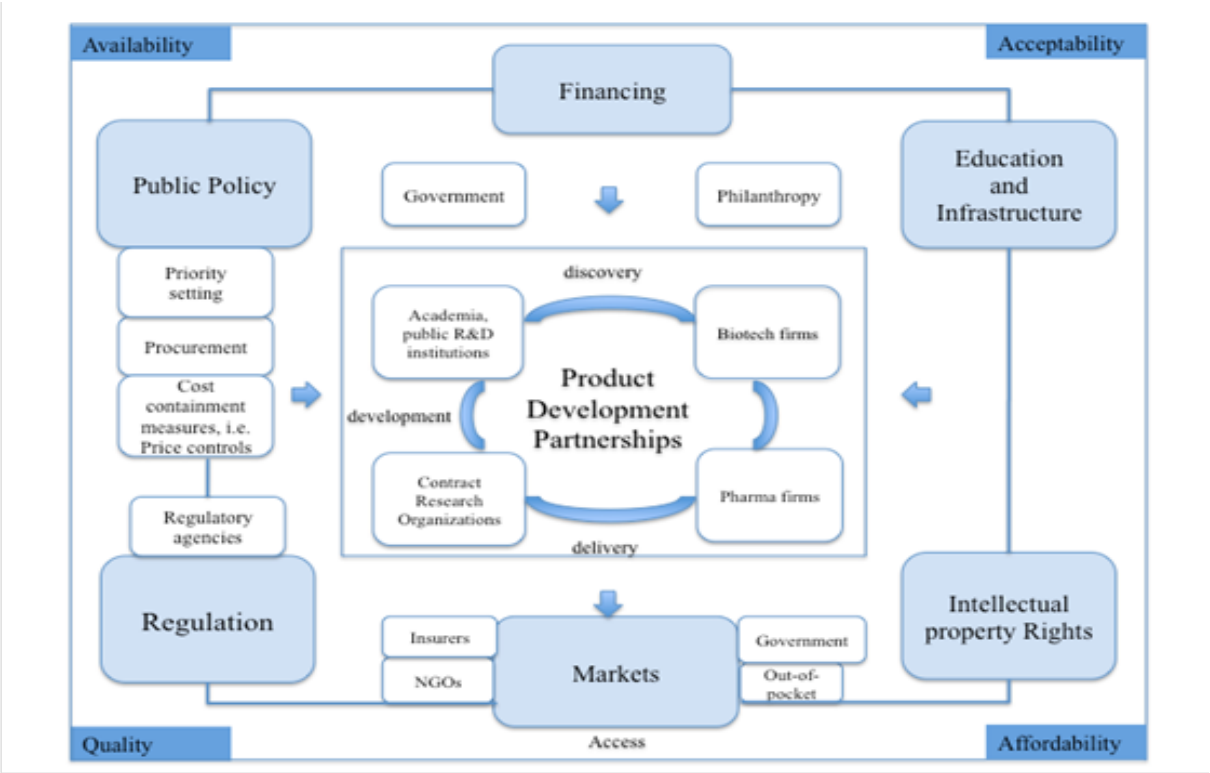
Evidence suggests that collaboration in R&D for neglected diseases is increasing. At now, there are around 348 organizations from private and public sector (academic/research institutions, biotechnology companies and other medium and small firms such as contract

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). There are no radical innovations right now, but the pipeline is promising.

As shown in Figure 1, PDPs are part of a broader R&D innovation ecosystem. PDPs play the role of ‘’system integrator’’ involving actors in any stage of the R&D chain and they operates in accordance with the following principles:

5) *Availability:* new product development and adequate supply (quantity) of product;
6) *Acceptability:* usability and appropriateness of the product tailored to specific needs;
7) *Quality:* product effectiveness, standards for carrying out testing and clinical trials;
8) *Affordability:* ensuring financing of product development and procurement, affordable prices.

Figure 1. PDPs in the Medical Product Innovation Ecosystem - Sources: Morel 2005, WHO 2006 (our elaboration)



PDP organizational form is not free of constrains. The study discussed the following ones:

- Constraints on the determinants of R&D productivity;
- Constraints on financing and priority setting;
- Constraints of access and delivery;
- Constraints of contracting and coordination problems; and
- Constraints of insufficient transparency.

How important is the IP management for a PDP? PDPs have different view on how IP should be managed and the second paper "Intellectual Property Management in Collaborative R&D: Non-Profit Medical Product Development Partnerships" tried to shed light on the issue.

The paper was elaborated on the basis of surveys. Sixteen PDPs answered the survey. This research finds that most of the PDPs have a clear IP policy that allow to them to clarify on how to operate, internally and externally with partners. Most PDPs that manage R&D portfolios (as opposed to financing PDPs) are users of intellectual property to access know how and technology that they require for building their R&D portfolios and to transfer technology to third parties. Access to access related know-how or capabilities of the patent holder is considered to be highly important, in addition to access to the patented technology. However, PDPs differ on whether or not they claim intellectual property rights. The more widely used form of intellectual property is patent, in order to ensure freedom to operate and to license patents to industry to raise their interest in partnering in manufacturing and distribution, and to avoid third parties from unauthorized use of the technology or claiming ownership of patents over the technology. Most PDPs consider that open R&D collaboration is useful. The discussion on terms for ownership of future patents is sometimes an obstacle for the successful conclusion of partnerships at any R&D stage.

We target to publish the full results of the study soon in a leading journal, pending target journal for publication is Research Policy.

II. Session 2: Interactive discussion

This session aimed at fostering a critical discussion on the themes of the project, and to give feedback to the project leaders on the research undertaken and unanswered questions for future research and policy action.

The panel was composed of representatives of various stakeholders involved in product-development partnerships (PDPs) for neglected diseases. These included an academic, a pharmaceutical industry expert, members of two product-development partnerships, and an expert involved in both research and policy-making on neglected diseases.

The panelists were the following:

1. Dominique Foray, Chair of Economics and Management of Innovation, EPFL (acting as Chair and moderator of the panel discussion)
2. Patrick Gaulé, Assistant Professor at CERGE, Czech Republic
3. Paul Herrling, Chair, Novartis Institute for Tropical Diseases
4. Jean François Alesandrini, Director of Policy and Fundraising, DNDi
5. Keith Neroutsos, Director of Procurement, and Steve Brooke, Advisor, Commercialization, PATH
6. Carlos Correa, Special Advisor on IP and Trade, South Centre

II.1 Summary of the discussion

The Chair, Dominique Foray, opened the discussion by noting that from an economic point of view, it is very important to understand to what extent are PDPs filling the R&D gap in

neglected diseases. PDPs are relatively new institutions that have tried to solve resource allocation problems through collaborations.

The discussion revolved around two questions.

II.1.1 To what extent have PDPs changed the operating framework for R&D in neglected diseases? Are PDPs a radical change?

It was noted that in the PDP framework is that in contrast to applied biomedical research by pharmaceutical firms where innovation is driven by a profit incentive, PDPs make resource allocation decisions based on health needs.

There are not economic factors that lead to the creation of PDPs. They are created for humanitarian reason to answer to a market failure. It was noted that PDPs respond to both a market failure as well as to a government failure in stimulating innovation in neglected diseases.

There were differences of opinion as to whether PDPs are a model of R&D and innovation, or whether they are still an experiment. In this context, it was also noted that it could be worth exploring whether the PDP scheme could be extended to apply more broadly to other medical product development beyond neglected diseases.

Overall, collaboration for innovation is not new. Public-private collaboration is also not new. What is new is the model in which a new institution (PDP) is coordinating public and philanthropic funding, academia and private firms towards the joint aim of creating new medical products to address public health needs. The innovation of PDPs is the system integrator function that PDPs play so that the right types of medical products are developed. PDPs coordinate different players to generate the pipeline.

Most PDP are involved in "virtual" medial product development in a "virtual" way, as most PDPs do not have in-house labs but rely on external collaborations for R&D activities. Nonetheless, there is wide variety among PDPs and it is difficult to define a single model.

An achievement of PDPs is that they have diverted some of the attention of academia and industry to the area of neglected diseases, to put to use modern technology and methods to translate basic science and generate a large pipeline of projects. PDPs leverage partnerships. It was noted that multinational pharmaceutical firms are likely to continue to collaborate with PDPs for different reasons in the short and long term. In the short term, the continued motivation is reputation. In the long term, it is about learning about how to work in the markets in emerging economies as a source of future customers and increased sales.

To date, PDPs have done mainly incremental innovation, but there is the prospect of breakthrough innovation, evidenced in the pipeline of products in Phase III trials. Nonetheless, it is not clear whether the pipeline will change dramatically. So far no new chemical entities have been developed and only 1% of all clinical trials are for neglected diseases. Moreover, new products for neglected diseases may be developed by PDPs or by other means.

II.1.2 What is the future of PDPs?

Diverse opinions were expressed in respect to the future of PDPs. Some panelists were of the view that the role of PDPs will continue to be important in the future, while others considered that PDPs are part of a transition phase and an experiment for the future way forward which is the production of medical products as public goods.

Panelists also debated whether the public sector could and should be taking up the role of PDPs. Some considered that public sector should indeed be more involved, as it is the role of public sector to produce public goods and could be playing a greater role in R&D. Others viewed that PDPs respond to the failure of public sector to act, and considered that PDPs have more flexibility to do the needed activities, utilize management practices of private sector, and considered that the private sector is better suited as compared to the public sector to carry out for translational research.

It was noted that the continued growth in the number of PDPs might not be useful. Successful PDPs should cease to exist once their work is finalized.

One panelist highlighted that the focus of PDPs should be on impact as the key factor, not on radical innovation as a principle but only when considered necessary. The repurposing of existing medical products can have significant therapeutic value for patients as can radical innovation.

All panelists raised concern on the future sustainability of PDPs. Financing of PDPs is not assured in the long term and there is a need to diversify donors, as currently many PDPs depend on single public donors or philanthropic foundations (i.e. Gates Foundation). It was noted that some PDPs are trying to diversity their funding sources. One mean described is to establishing a target of not more than 25% of funding from a single donor in order to avoid dependence and manage risk. It was also noted that there is a need to increase social venture capital.

Panelists also discussed the role of philanthropic donors, particularly the Gates Foundation as the major philanthropic donor of PDPs, in terms of the future sustainability of PDPs and its role in defining priorities, models of innovation and access criteria. It was noted that medical product donations are a parallel short-term strategy for disease eradication that is being implemented by philanthropic organizations, and concern was expressed by some of the impact of this strategy in the long term.

Panelists identified various improvements that could be made to the current way in which PDPs operate. These included increasing collaboration and overall transparency on the costs of R&D, the failures experienced, results of clinical trials, the terms of the contracts with partners and donor funding. It was also noted that currently there is competition among PDPs, for example in Malaria. As donors provide financing, and a single philanthropic donor provides a significant amount of the financing, there is significant pressure on PDPs to show outcomes and ownership of results associated to the PDP. However, this competition may not always be supportive of the objectives PDPs seek to achieve. It was noted that there is a need to increase collaboration among PDPs and seek more complementarities. It was further noted that there is a need for a forum to promote discussion and increase communication among PDPs. Some panelists were of the view that donors should put resources into promoting increased collaboration among PDPs, rather than PDPs investing their resources in this activity. It was noted that because PDPs receive financing from donors is received based on a competitive selection, all elements in the financing proposals are presented are core activities of the PDP, and as such there are no additional resources for non-core activities such as promoting collaboration.

Panelists discussed intellectual property management by PDPs. Most participants were of the view that a defined policy on intellectual property serves to provide clarity from the beginning of a project and speeds up negotiations with partners. However, there were different views on the content of intellectual property policies. One panellist observed that in the case of one PDP, the medical product to be developed is considered to be a public good so no patent can be taken out on that product by the PDP for the specific indication. Another view expressed was that intellectual property is a tool that can be used as a tool for access, as well as a tool that can be abused. It was also noted that commercial firms may place limitations on intellectual property but there are ways to work around the limitations so that it does not impede work by the PDP.

It was noted that some PDPs are building on open innovation as a means to avoid overlap, duplication and to speed up research and development.

Panelists noted that capacity building in endemic countries was important, including increasing their ability to participate in R&D and innovation. There were different views expressed on the extent to which PDPs currently play a role in building these capacities, and to what extent PDPs should have this role or not.

II.2. Recommendations

From the discussions, a number of recommendations were suggested:

1) Need for global coordination, priority setting, and resource allocation to R&D in neglected diseases.

It was noted that priorities should be defined based on public health needs, including defining a target product profile and ensuring the product developed will be affordable. It was also noted there is a lack of oversight and evaluation of the overall R&D pipeline on neglected diseases, and potentially waste, duplication and competition among efforts.

It was suggested that there is a role for the WHO. It was emphasized that the needed public leadership role and cooperation among governments is not only limited to increasing the financial resources available, but in coordinated priority setting and oversight.

2) Need for increased coordination among PDPs.

It was noted that there is little coordination among the many PDPs operating independently. It was considered that improved coordination among PDPs and other efforts on R&D in neglected diseases would lead to better strategy for the overall R&D pipeline and use of resources. It was also noted that there is a feeling of competition among PDPs in the search for donor financing.

It was suggested that a platform be established where PDPs could talk and learn from each other, to identify redundancy and complementarities. Some noted that funders and governments should promote elaborating such platform, as PDPs have limited capacities and resources for promoting greater inter-PDP collaboration.

3) Need for greater transparency and accountability of all actors involved in R&D for neglected diseases.

It was noted that there is precise data on the cost of making new medical products and large variability on estimations and the data presented by different actors. In the case of PDPs, it was noted with interest that PDPs appear to be contributing to finding more efficient and less costly ways to operate. The example of some PDPs setting a target price upfront to ensure affordability and uptake was cited as a good practice. However, there is also limited information about the costs of PDP projects and resource allocated to partners.

It was suggested that the framework for collaboration and priority setting suggested above for the WHO should also promote greater transparency and accountability of PDPs and other actors involved in R&D for neglected diseases.

4) Need for increased government support for a sustainable solution.

Currently R&D in neglected diseases depends to a large extent from donor and philanthropic financing. It was noted that continued reliance on donor funding in the long term it is not sustainable, as donor and philanthropic priorities for funding may change, and it is not provided on a short-term or medium term based on specific projects. Thus, there is a need to seek more stable funding. It was considered that it is a responsibility of governments to provide and maintain some guarantees of funding.

5) Need to build capabilities in endemic countries.

It was identified that there is a need for a concerted program / plan of action to develop the capacities of endemic countries for R&D in neglected diseases, under government leadership through the WHO. The work of PDPs should be integrated to this program, so that PDPs also contribute to this aim.