Research Synthesis: Product Development Partnerships

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Introduction

The literature around product development partnerships is considerable*, with a focus on the structure adopted by Product Development Partnerships (PDPs) and analysis of specific initiatives.

Search terms

Product Development Partnership

Synthesis of the literature

The goal of PDPs is to develop new, public health-related medical products tapping into the research and development assets and skills of multiple actors. PDPs started to form in the mid-1990s, beginning with the International AIDS Vaccine Initiative and Medicines for Malaria Venture (Abuduxike and Aljunid 2012). The World Health Organization's Special Programme for Research and Training in Tropical Diseases (TDR) played a central role in the emergence of PDPs by providing an international framework for coordinating infectious disease research activities in the decades prior. In addition, philanthropic foundations, in particular the Bill and Melinda Gates Foundation and Rockefeller Foundation, helped establish and maintain the existence of PDPs (Munoz et al. 2015).

Features/Characteristics

PDPs are usually non-profit entities that have separate and distinct legal personalities. They are characterized as collaboration partnerships between public and private sector parties (Kulkarni et al. 2015) and usually use a "multi-candidate/portfolio approach" in addressing poverty-related diseases (Technopolis Group 2014). PDPs often involve entities in countries where the targeted diseases are endemic (Burrows et al. 2014). PDPs focus on neglected diseases affecting developing countries -- categorized by WHO as Types II and III," or those that mostly affect poor populations (Billington 2016). The non-profit character of PDPs allows them to operate without shareholder or profit requirements. However, it is noted that they rely on funding from external parties to achieve their purpose (Bishai et al. 2011). It has also been noted that PDPs often share the monetary burden and uncertainties with their partners with respect to drug development (Burrows et al. 2014). Munoz et al. (2015) provide a detailed analysis of the governance structure and limitations of PDPs, the latter including, e.g. adequate financing for new chemical entities, level of skill of PDP project managers and organization size, unclear

agenda setting processes, and lack of transparency (Munoz et al. 2015). Another paper focused on the PDP "development and management" processes (De Pinho Campos, Norman, and Jadad 2011). Two papers described the collaborations with partners of PDPs (Bio Ventures for Global Health 2012; Grace 2010). Ziemba (2005) focused on critical areas that impact the success of PDPs, such as financing and governance structure. It is noted in the study that there is minimal representation of developing countries in the PDP Boards and committees, and that PDPs should seek funding from developing countries, who are the target recipients of the products, among other possible sources of funds (Ziemba 2005).

PDPs have been referred to as "virtual organizations" (Technopolis Group 2014; Munoz et al. 2015), "virtual R&D" (Billington 2016), "system integrators" (Munoz et al. 2015), and "integrator or knowledge broker" (Huzair 2012) since they do not usually engage in hands-on R&D activities but instead coordinate and collaborate with partners who perform said activities (Munoz et al. 2015). PDPs usually develop multiple drugs or medical technologies simultaneously, which allow them to hedge against potential failures of some of their product development projects (Billington 2016).

PDPs adopt individual policies to ensure access to the resulting medical products by those who need them (Munoz et al. 2015). A common PDP objective is guaranteeing the affordability of the resulting medical product to the target patient populations, who are usually in low and middle income countries (Billington 2016). PDPs' focus on affordable and accessible drugs advances the concept of R&D for health "as a global public good" (Keusch et al. 2010). However, it has been observed that PDPs widely differ with respect to their approaches to managing intellectual property (Munoz et al. 2015).

PDP Organizations

Some of the literature focuses on specific PDP organizations. A sampling of PDP initiatives are available:http://www.technopolisgroup.com/wpcontent/uploads/2014/11/141118_PDP_Review_Technopolis_Group4.pdfand https://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf.

Drugs for Neglected Diseases initiative (DNDi) is one of the larger PDPs and has developed 6 new products in a relatively short period of time (Médecin Sans Frontières 2013). DNDi is noted for its non-exclusive license agreements and cost-plus product pricing contractual stipulations that facilitate long-term access to the resulting medical technologies (World Health Organization, World Intellectual Property Organization and World Trade Organization 2012). Sabin Vaccine Institute and the Infectious Disease Research Institute, among other PDPs, have been credited for spearheading vaccine development for neglected tropical diseases (Beaumier et al. 2013). Huzair (2012) identified the World Health Organization-led "influenza vaccine innovation system" as a PDP, which however is unique from other PDPs because it has WHO as its main controlling and guiding entity (Huzair 2012). Hanlin noted the character of the South African AIDS Vaccine Initiative as a national, rather than the more usual international, PDP (Hanlin 2006).

Several studies analyzed specific projects carried out by PDPs. Gordon, Røttingen, and Hoffman (2014) provided a case study on the creation of the Meningitis Vaccine Project (MVP), and the development of the MenAfriVac vaccine, which involved multiple public and private partners including the WHO and PATH (Gordon, Røttingen, and Hoffman 2014). The strategy for the

MenAfriVac vaccine project was mainly influenced by the demand from African governments for a sustainable price of US$0.50 per dose (Gordon, Røttingen, and Hoffman 2014; Kulkarni et al. 2015; Bishai et al. 2011). Kulkarni et al. (2015) noted that the project succeeded due to the important factors of "transparency and an intense and close collaboration" of the parties, which allowed for proper know-how and technology transfer, i.e. crucial non-exclusive patent licenses for needed technology (Kulkarni et al. 2015). Bishai et al. (2011) emphasized the MVP's organizational structure, which is described as having a lattice form, and the willingness of businesses based in developing countries to undertake projects of PDPs for reasons other than profit. MVP showcased the ability of PDPs to facilitate transfer of technology and ensure affordability of medical technology (Bishai et al. 2011). Ubben and Poll (2013) focused on the development process for the drug Eurartesim undertaken by Medicines for Malaria Venture and its partner, emphasizing the collaborative strength in the PDP model (Ubben and Poll 2013). Luiza et al. (2017) and Wells, Diap, and Kiechel (2013) analyzed the drug development process of ASMQ-FDC, an anti-malaria drug developed by DNDi and its partners (Luiza et al. 2017; Wells, Diap, and Kiechel 2013).

Funding

The annual G-FINDER studies provide detailed, regularly-updated information on funding for PDPs (and for neglected disease R&D more broadly). Based on the 2017 G-Finder Report, USD 420 million was invested in PDPs in 2016, which was the least amount noted for PDP funding since 2007. 75% of this amount was directed to tackling HIV/AIDS, malaria and tuberculosis. Gates Foundation funding to PDPs dropped in 2016, yet it still accounted for the largest proportion of overall PDP funding at 54%. The sources of PDP funding in 2016 were philanthropic organizations, governments of high income countries and multilateral organizations, providing 57%, 39% and 3.4% of the funds respectively. PDP funding in the past 10 years followed a similar pattern with the Gates Foundation and bilateral aid agencies providing the bulk of finances at close to 90%. However, funding levels in 2016 may be influenced by the fact that PDPs follow funding cycles. At least 40-50% of the yearly PDP funding went to the 3 PDPs receiving the most funds for that year, which in 2016 were the International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV) and Programme for Appropriate Technology in Health (PATH). In the past 10 years, PATH was the PDP that received the most funding (Chapman et al. 2017). Tables indicating the amounts and sources of PDP funding for the period 2007 to 2016 are available at http://policycuresresearch.org/downloads/Y10_G- FINDER_full_report.pdf.

Results

Meredith and Ziemba (2008) noted that PDPs have led 85% of the R&D for 106 neglected disease products since 2000 (Meredith and Ziemba 2008). PDP drug development projects initially focused mainly on drug repurposing. It has been noted that while PDPs had several new chemical entities (NCE) in clinical trials (Munoz et al. 2015), there were relatively few that had been brought to market. We found three PDP-developed NCEs: Pretomanid developed by the TB Alliance[1], Dihydroartemisinin-piperaquine (Eurartesim) developed by MMV[2], and Fexinidazole for sleeping sickness developed by DNDi[3].

Munoz et al. (2015) provide a table of PDPs and the diseases they tackle as well as a list of PDPs and the drugs they developed. Malaria has been noted to be the top disease tackled by PDPs (Munoz et al. 2015). Abuduxike and Aljunid (2012) included a brief numerical summary of the products being developed by PDPs in 2009, categorized according to their development stage (Abuduxike and Aljunid 2012). Young et al. (2018) used a modified Portfolio to Impact model to

approximate the costs and launches of 538 out of the 685 product candidates identified from the neglected disease pipeline (Young et al. 2018).

Limitations/Critiques

Munoz et al. (2015) argued that donors determine the priority areas for drug R&D and the terms governing the use of funds. Because PDPs rely on donors for funding, there may be a dissonance between the priorities of donors and disease-endemic countries. Further, since PDPs rely on short- term funds, their long-term financial viability is uncertain and affected by financial pressures on their donors. Furthermore, the extent to which PDPs collaborate with each other is generally not publicly- visible, and may result in unnecessary inefficiencies (Munoz et al. 2015).

Huzair (2012) suggested that PDPs may benefit from having a main knowledge and coordinating entity (Huzair 2012). Bishai et al. (2011) have argued that PDPs must have a flexible, more disaggregated project structure, engage public laboratories as possible resources for technologies similar to the US Food and Drug Administration's Center for Biologics Evaluation and Research, as well as engage more the WHO in their projects in order to benefit from its technical expertise and relationships with international and national actors (Bishai et al. 2011). Årdal, Alstadsæter, and Røttingen (2011) suggested that PDPs should finance more open source drug discovery projects, and noted that some PDPs, to a certain extent, already use open-source mechanisms in their R&D processes (Årdal, Alstadsæter, and Røttingen 2011).

Others

Bhatia and Narain (2010) and Billington (2016) suggested a PDP model to tackle the need for new antibiotics R&D (Bhatia and Narain 2010, Billington 2016); in 2016 the Global Antibiotic R&D Partnership (GARDP) was created for this purpose.

1. "Our Pipeline – Pretomanid," TB Alliance, accessed on 30 October 2018,https://www.tballiance.org/portfolio/compound/pretomanid.
2. "Frequently asked questions about Eurartesim," Medicines for Malaria Venture, accessed on 30 October 2018,https://www.mmv.org/access/products-projects/eurartesim-dihydroartemisinin- piperaquine/frequently-asked-questions-about.
3. "Fexinidazole (HAT)," Drug for Neglected Diseases Initiative, accessed on 30 October 2018, https://www.dndi.org/diseases-projects/portfolio/fexinidazole/.

Research gaps

- Updated analysis of the successes and failures of PDPs, especially on new chemical entities developed by PDPs
- Operational costs of PDPs, in general, and costs specific to PDP R&D activities
- Analysis of intellectual property and access policies and practices of PDPs
- More information on the governance structure and processes of PDPs and the impact it can have on their decisions

Cited papers with abstracts

Abuduxike, Gulifeiya, and Syed Mohamed Aljunid. 2012. “Development of Health Biotechnology in Developing Countries: Can Private-Sector Players Be the Prime Movers?” Biotechnology Advances 30 (6): 1589–1601. https://doi.org/10.1016/j.biotechadv.2012.05.002.

Abstract: Health biotechnology has rapidly become vital in helping healthcare systems meet the needs of the poor in developing countries. This key industry also generates revenue and creates employment opportunities in these countries. To successfully develop biotechnology industries in developing nations, it is critical to understand and improve the system of health innovation, as well as the role of each innovative sector and the linkages between the sectors. Countries' science and technology capacities can be strengthened only if there are non-linear linkages and strong interrelations among players throughout the innovation process; these relationships generate and transfer knowledge related to commercialization of the innovative health products. The private sector is one of the main actors in healthcare innovation, contributing significantly to the development of health biotechnology via knowledge, expertise, resources and relationships to translate basic research and development into new commercial products and innovative processes. The role of the private sector has been increasingly recognized and emphasized by governments, agencies and international organizations. Many partnerships between the public and private sector have been established to leverage the potential of the private sector to produce more affordable healthcare products. Several developing countries that have been actively involved in health biotechnology are becoming the main players in this industry. The aim of this paper is to discuss the role of the private sector in health biotechnology development and to study its impact on health and economic growth through case studies in South Korea, India and Brazil. The paper also discussed the approaches by which the private sector can improve the health and economic status of the poor.

Link: https://www.sciencedirect.com/science/article/pii/S0734975012001024

Årdal, Christine, Annette Alstadsæter, and John-Arne Røttingen. 2011. “Common Characteristics of Open Source Software Development and Applicability for Drug Discovery: A Systematic Review.” Health Research Policy and Systems 9 (1). https://doi.org/10.1016/j.biotechadv.2012.05.002.

Abstract: Background: Innovation through an open source model has proven to be successful for software development.This success has led many to speculate if open source can be applied to other industries with similar success. We attempt to provide an understanding of open source software development characteristics for researchers, business leaders and government officials who may be interested in utilizing open source innovation in other contexts and with an emphasis on drug discovery.

Methods: A systematic review was performed by searching relevant, multidisciplinary databases to extract empirical research regarding the common characteristics and barriers of initiating and maintaining an open source software development project.

Results: Common characteristics to open source software development pertinent to open source drug discovery were extracted. The characteristics were then grouped into the areas of

participant attraction, management of volunteers, control mechanisms, legal framework and physical constraints. Lastly, their applicability to drug discovery was examined.

Conclusions: We believe that the open source model is viable for drug discovery, although it is unlikely that it will exactly follow the form used in software development. Hybrids will likely develop that suit the unique characteristics of drug discovery. We suggest potential motivations for organizations to join an open source drug discovery project. We also examine specific differences between software and medicines, specifically how the need for laboratories and physical goods will impact the model as well as the effect of patents.

Link: https://health-policy-systems.biomedcentral.com/articles/10.1186/1478-4505-9-36

Bhatia, Rajesh and Jai P. Narain. 2010. "The Growing Challenge of Antimicrobial Resistance in the South-East Asia Region - Are We Losing the Battle." The Indian Journal of Medical Research 132 (November): 482–86.

Abstract: Not available

Link: http://www.ijmr.org.in/temp/IndianJMedRes1325482-3446526_093425.pdf

Billington, John K. 2016. "A New Product Development Partnership Model for Antibiotic Resistance." American Journal of Law & Medicine 42 (2-3): 487-523. https://doi.org/10.1016/j.biotechadv.2012.05.002.

Abstract: Antibiotics have prevented countless deaths from common infections and have made possible many modern medical procedures. Over the past few decades, antibiotic-resistant bacteria have become a global threat, spreading between healthcare facilities and throughout communities worldwide at an alarming pace. Antibiotic overuse and misuse in humans, animals, and the environment accelerate resistance by selecting for bacteria with antibiotic-resistant traits, which then become predominant and infect others. Meanwhile, few antibiotics remain active against the most resistant bacteria. There is an urgent need for new antibiotics and other antibacterial products to replace second-line and last resort therapies when they no longer work. This Article proposes a new U.S.-based, non-governmental, not-for-profit product development partnership (PDP) model specifically designed for antibacterial development. This new model should both supplement and complement existing government-led efforts and should be built with mechanisms in place to balance the values of innovation, access, and conservation.

Link: http://journals.sagepub.com/doi/abs/10.1177/0098858816658277

Bio Ventures for Global Health. 2012. "Developing New Drugs and Vaccines for Neglected Diseases of the Poor: The Product Developer Landscape."

Abstract: Not available

Link: Not available

Bishai, David M., Claire Champion, Michael E. Steele, and Lindsay Thompson. 2011. “Product Development Partnerships Hit Their Stride: Lessons From Developing A Meningitis Vaccine For Africa.” Health Affairs 30 (6): 1058–64. https://doi.org/10.1016/j.biotechadv.2012.05.002.

Abstract: The Meningitis Vaccine Project, a so-called product development partnership, developed a new vaccine against bacterial meningitis, an inflammation of brain tissues that causes an estimated 10,000 deaths among African children and young people each year. The vaccine—known as MenAfriVac and specifically targeted for use in low-income countries in Africa—was designed to be made available to governments at a price of fifty cents per dose. The Meningitis Vaccine Project is an example of how product development partnerships have reinvigorated research on vaccines for neglected diseases. These partnerships disperse the multiple tasks of product development across a network of partners that are best suited for each task. The vaccine was rapidly embraced by African
health officials, and in its first few weeks on the market, in late 2010, more than nineteen million people in Burkina Faso, Mali, and Niger were vaccinated.

Link: https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2011.0295

Burrows, Jeremy N., Richard L. Elliott, Takushi Kaneko, Charles E. Mowbray, and David Waterson. 2014. “The Role of Modern Drug Discovery in the Fight against Neglected and Tropical Diseases.” MedChemComm 5 (6): 688. https://doi.org/10.1039/c4md00011k.

Abstract: Not available

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Chapman, Dr Nick, Anna Doubell, Lisette Oversteegen, Dr Vipul Chowdhary, Dr George Rugarabamu, Renata Zanetti, Ming Ong, and Juliette Borri. 2017. "Neglected Disease Research and Development: Reflecting on a Decade of Global Investment.” Policy Cures Research. http://policycuresresearch.org/downloads/Y10_G-FINDER_full_report.pdf.

Abstract: Not available

Link: http://policycuresresearch.org/downloads/Y10_G-FINDER_full_report.pdf

De Pinho Campos, Katia, Cameron D. Norman, and Alejandro R. Jadad. 2011. “Product Development Public–Private Partnerships for Public Health: A Systematic Review Using Qualitative Data.” Social Science & Medicine 73 (7): 986–94. https://doi.org/10.1016/j.socscimed.2011.06.059.

Abstract: Almost a decade ago, public health initiated a number of innovative ventures to attract investments from multinational drug companies for the development of new drugs and vaccines to tackle neglected diseases (NDs). These ventures - known as product development public–private partnerships (PD PPPs) - represent the participation of the public and private actors toward the discovery and development of essential medicines to reduce the suffering of over one billion people worldwide living with NDs. This systematic review aimed to identify empirical-based descriptive articles to understand critical elements in the partnership process, and propose a

framework to shed light on future guidelines to support better planning, design and management of existing and new forms of PPPs for public health. Ten articles met the inclusion criteria and were analyzed and synthesized using qualitative content analysis. The findings show that the development stage of PD PPPs requires a careful initiation and planning process including discussion on values and shared goals, agreement on mutual interests & equality of power relation, exchange of expertise & resources, stakeholder engagement, and assessment of the local health capacity. The management stage of PD PPPs entails transparency, extensive communication and participatory decision-making among partner organizations. This review illustrates the difficulties, challenges and effective responses during the partnering process. This model of collaboration may offer a way to advance population health at present, while creating streams of innovation that can yield future social and financial dividends in enhancing the public's health more widely.

Link: https://www.sciencedirect.com/science/article/pii/S0277953611004278

Gordon, Rachel, John-Arne Røttingen, and Steven Hoffman. 2014. "The Meningitis Vaccine Project," 15.

Abstract: Not available

Link:
https://caseresources.hsph.harvard.edu/files/case/files/2014_meningitis_vaccine_project_0.pdf

Grace, Cheri. 2010. "Product Development Partnerships (PDPs): Lessons from PDPs Established to Develop New Health Technologies for Neglected Diseases." https://assets.publishing.service.gov.uk/media/57a08b29ed915d3cfd000b90/Lessons_Learded_from_ PDPs Report.pdf.

Abstract: Not available

Link:
https://assets.publishing.service.gov.uk/media/57a08b29ed915d3cfd000b90/Lessons_Learded_from_PDPs Report.pdf

Hanlin, Rebecca. 2006. "Increasing Knowledge Flows by Linking Innovation and Health - the Case of SAAVI." Genomics, Society and Policy 2 (3). https://doi.org/10.1186/1746-5354-2-3-37.

Abstract: Biotechnology and genomic innovation are seen as increasingly important for achieving public health goals in Africa. In particular, vaccines based on advances in genomic technology are deemed vital in the fight against HIV/AIDS. Public-Private Partnerships (PPPs) provide a collaborative mechanism to ensure these vaccines are developed when the private sector lacks incentives to develop these products. These partnerships provide new mechanisms for transferring the knowledge required to ensure vaccine development occurs as quickly and efficiently as possible. One such accine partnership is the South African AIDS Vaccine Initiative (SAAVI). This has been successful in ensuring 'value added' (benefit gained by taking part) is created for those involved particularly in the area of intangible value added determinants of collaboration and knowledge capacity. This paper outlines the results of a case study of SAAVI and

argues that it provides evidence of a need to strengthen our understanding of the linkage between wider conceptual 'systems' of innovation and health. In particular, it espouses the usefulness of 'Systems of Innovation' thinking as a means to ensure that more specific focus is placed on process outputs such as collaboration and knowledge capacity. This will ensure that necessary knowledge flow is transferred between those working in the vaccine project for more efficient and effective operations. The research also raises questions about the possibility of such case studies highlighting areas of attention that need addressing if greater linkage is to occur between innovation and health at a wider health research policy level.

Link: https://link.springer.com/article/10.1186/1746-5354-2-3-37

Huzair, Farah. 2012. “The Influenza Vaccine Innovation System and Lessons for PDPs.” Human Vaccines & Immunotherapeutics 8 (3): 407–10. https://doi.org/10.4161/hv.18701.

Abstract: As Product Development Partnerships (PDPs) emerge and evolve in response to the need for vaccines, this paper re-examines the oldest and most successful PDP in the vaccine field; that which year after year, produces and reinvents influenza vaccines. This paper describes the influenza vaccine production and innovation system and reviews some of its most recent major innovations. Innovation in this system is a result of collaborative partnerships between various actors from both the public and private sector. It is argued that the influenza vaccine innovation system is a Product Development Partnership (PDP), be it an unconventional one, with a central coordination role allocated to the WHO rather than a private company or charitable/not for profit entity. The unusual structure of this PDP overcomes some of the organizational issues surrounding vaccine research and production faced by other documented PDPs. These are first, the need to coordinate knowledge flow via an effective knowledge broker. Second, the need to build in-house capacity and fund essential research and elements of production where private partners find involvement too risky or costly.

Link: https://www.tandfonline.com/doi/abs/10.4161/hv.18701

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Kulkarni, Prasad S., Muriel Socquet, Suresh S. Jadhav, Subhash V. Kapre, F. Marc LaForce, and Cyrus S. Poonawalla. 2015. “Challenges and Opportunities While Developing a Group A Meningococcal Conjugate Vaccine Within a Product Development Partnership: A Manufacturer’s Perspective From the Serum Institute of India.” Clinical Infectious Diseases 61 (suppl_5): S483–88. https://doi.org/10.1093/cid/civ500.

Abstract: Background. In 2002, the Meningitis Vaccine Project (MVP) chose the Serum Institute of India, Ltd (SIIL), as its manufacturing partner to establish a product development partnership (PDP) with the Meningitis Vaccine Project (MVP). MVP was a collaboration between PATH and the World Health Organization (WHO) to develop meningococcal conjugate vaccines for sub-Saharan Africa.

Method. From the outset, SIIL recognized that a partnership with MVP carried some risk but also offered important opportunities for accessing new conjugate vaccine technology and know-how. Over
3 years, SIIL successfully accepted technology transfer for the group A meningococcal polysaccharide from SynCo Bio Partners and a conjugation method from the US Food and Drug Administration.

Results. SIIL successfully scaled up production of a group A meningococcal conjugate vaccine that used SIIL tetanus toxoid as the carrier protein. Phase 1 studies began in India in 2005, followed by phase 2/3 studies in Africa and India. A regulatory dossier was submitted to the Indian authorities in April 2009 and WHO in September 2009. Export license was granted in December 2009, and WHO prequalification was obtained in June 2010. Vaccine was introduced at public scale in Burkina Faso that December. The group A meningococcal conjugate vaccine was named MenAfriVac, and is the first internationally qualified vaccine developed outside of big pharma.

Conclusions. The project proved to be a sound investment for SIIL and is a concrete example of the potential for PDPs to provide needed products for resource-poor countries.

Link: https://academic.oup.com/cid/article/61/suppl_5/S483/417594

Luiza, Vera Lucia, Gabriela Costa Chaves, Tayná Marques Torres Barboza, Luciana de Paula Barros Gonçalves, and Eric G. Stobbaerts. 2017. “Desafios de Uma Parceria Para o Desenvolvimento de Produtos: O Caso de Um Tratamento Para Malária.” Ciência & Saúde Coletiva 22 (7): 2197–2211. https://doi.org/10.1590/1413-81232017227.04042017.

Abstract: This paper examines the development of a treatment – a fixed-dose combination of artesunate and mefloquine – in Brazil, from three points of view: in terms of access to medication; to record and report successes; and to look at the lessons learned. This product development took place in the ambit of a public-private partnership. Semi-structured interviews were held with key actors involved in the different phases of the development, and documents were analyzed. Two important points of reference orienting the design of the study and analysis were: a logical model for access to medication; and evaluation of programs. It is concluded that there were several successes over the course of the project, but insufficient attention was given in the project’s architecture to planning of adoption of the product: irregularities in demand caused difficulties in planning and production, and adoption of the product was irregular in the Americas. It is concluded that the project can be considered to have been successful: the product was created, and the aims were met – strengthening of institutional and individual capacities and alliances, and advocacy. However, there were weaknesses in the process, which need to be mitigated in future projects of the same type.

Link: http://www.scielo.br/scielo.php?script=sci_abstract&pid=S1413-81232017002702197&lng=en&nrm=iso&tlng=en

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Abstract: Not available

Link: https://www.msf.org/dndi-ten-past-success-future-challenges

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Abstract: Not available

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Munoz, V., F. Visentin, D. Foray, and P. Gaule. 2015. “Can Medical Products Be Developed on a Non-Profit Basis? Exploring Product Development Partnerships for Neglected Diseases.” Science and Public Policy 42 (3): 315–38. https://doi.org/10.1093/scipol/scu049.

Abstract: 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 paper contributes to an understanding of R&D in a non-profit context and highlights the importance of collaboration and non- market institutions for promoting innovation where market failures occur.

Link: https://academic.oup.com/spp/article/42/3/315/1628840

Technopolis Group. 2014. “Review of the Product Development Partnerships Fund 2011-2014: Final Report to the Dutch Ministry of Foreign Affairs.” http://www.technopolis-group.com/wp-content/uploads/2014/11/141118_PDP_Review_Technopolis_Group4.pdf.

Abstract: Not available

Link: http://www.technopolis-group.com/wp-content/uploads/2014/11/141118_PDP_Review_Technopolis_Group4.pdf

Ubben, David, and Elizabeth M Poll. 2013. “MMV in Partnership: The Eurartesim® Experience.” Malaria Journal 12 (1). https://doi.org/10.1186/1475-2875-12-211.

Abstract: Background: This case study describes how a public-private partnership between Medicines for Malaria Venture (MMV) and Sigma-Tau Industrie Farmaceutiche Riunite SpA achieved international regulatory approval for use of the fixed-dose artemisinin-based combination therapy dihydroartemisinin-piperaquine (Eurartesim®) for the treatment of malaria, enabling more widespread access to the medicine in malaria-endemic countries.

Case description: The combination of dihydroartemisinin and piperaquine demonstrated success in clinical trials for the treatment of malaria in Asia and Africa in the2000s. However, as it had not been developed to international regulatory standards it was out of the reach of the majority of patients in disease-endemic countries, particularly those reliant on public healthcare systems supported by international donor funding. To overcome this, as of2004 MMV worked in partnership with Sigma-Tau, Holleykin, Oxford University,the Institute of Tropical Medicine Antwerp, and the National Institute of Malaria Research India to develop the dihydroartemisinin-piperaquine combination to international standards. In 2011, the European Commission granted full marketing authorization to Sigma-Tau for Eurartesim.

Discussion and evaluation: The partnership between MMV, Sigma-Tau, and numerous other academic and industrial partners across the world, led to the successful development to EMA regulatory standards of a high-quality and highly efficacious anti-malarial treatment that otherwise would not have been possible. The dossier has also been submitted to the WHO for prequalification, and a safety statement to guide correct use of Eurartesim has been produced. In July 2012, the first delivery to a disease-endemic country was made to Cambodia, where the medicine is being used to treat patients and help counter the emergence of artemisinin resistance in the area. A paediatric dispersible formulation of Eurartesim is being developed, with the objective to submit the dossier to the EMA by the end of 2014.

Conclusions: The development of Eurartesim to international regulatory standards exemplifies the strengths of the product development partnership model in utilising the individual skills and expertise of partners with differing objectives to achieve a common goal. Successful uptake of Eurartesim by public health systems in malaria-endemic countries poses new challenges, which may require additional partnerships as we move forward.

Link: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-12-211

Wells, Susan, Graciela Diap, and Jean-René Kiechel. 2013. “The Story of Artesunate–Mefloquine (ASMQ), Innovative Partnerships in Drug Development: Case Study.” Malaria Journal 12 (1): 68. https://doi.org/10.1186/1475-2875-12-68.

Abstract: Background: The Drugs for Neglected Diseases initiative (DNDi) is a not-for profit organization committed to providing affordable medicines and access to treatments in resource-poor settings. Traditionally drug development has happened “in house” within pharmaceutical companies, with research and development costs ultimately recuperated through drug sales. The development of drugs for the treatment of neglected tropical diseases requires a completely different model that goes beyond the scope of market-driven research and development.

Artesunate and mefloquine are well-established drugs for the treatment of uncomplicated malaria, with a strong safety record based on many years of field-based studies and use. The administration of such artemisinin-based combination therapy in a fixed-dose combination is expected to improve patient compliance and to reduce the risk of emerging drug resistance.

Case description: DNDi developed an innovative approach to drug development, reliant on strong collaborations with a wide range of partners from the commercial world, academia, government institutions and NGOs, each of which had a specific role to play in the development of a fixed dose combination of artesunate and mefloquine.

Discussion and evaluation: DNDi undertook the development of a fixed-dose combination of artesunate with mefloquine. Partnerships were formed across five continents, addressing formulation, control and production through to clinical trials and product registration, resulting in a safe and efficacious fixed dose combination treatment which is now available to treat patients in resource-poor settings. The south-south technology transfer of production from Farmanguinhos/Fiocruz in Brazil to Cipla Ltd in India was the first of its kind. Of additional benefit was the increased capacity within the knowledge base and infrastructure in developing countries.

Conclusions: This collaborative approach to drug development involving international partnerships and independent funding mechanisms is a powerful new way to develop drugs for tropical diseases.

Link: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-12-68

World Health Organization, World Intellectual Property Organization and World Trade Organization. 2012. "Promoting Access to Medical Technologies and Innovation: Intersections between Public Health, Intellectual Property and Trade." https://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf.

Abstract: Not available

Link: https://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf

Young, Ruth, Tewodros Bekele, Alexander Gunn, Nick Chapman, Vipul Chowdhary, Kelsey Corrigan, Lindsay Dahora, et al. 2018. “Developing New Health Technologies for Neglected Diseases: A Pipeline Portfolio Review and Cost Model.” Gates Open Research 2 (August): 23. https://doi.org/10.12688/gatesopenres.12817.2.

Abstract: Background: Funding for neglected disease product development fell from 2009-2015, other than a brief injection of Ebola funding. One impediment to mobilizing resources is a lack of information on product candidates, the estimated costs to move them through the pipeline, and the likelihood of specific launches. This study aimed to help fill these information gaps.

Methods: We conducted a pipeline portfolio review to identify current candidates for 35 neglected diseases. Using an adapted version of the Portfolio to Impact financial modelling tool, we estimated the costs to move these candidates through the pipeline over the next decade and the

likely launches. Since the current pipeline is unlikely to yield several critical products, we estimated the costs to develop a set of priority "missing" products.

Results: We found 685 neglected disease product candidates as of August 31, 2017; 538 candidates met inclusion criteria for input into the model. It would cost about $16.3 billion (range $13.4-19.8B) to move these candidates through the pipeline, with three-quarters of the costs incurred in the first 5 years, resulting in about 128 (89-160) expected product launches. Based on the current pipeline, there would be few launches of complex new chemical entities; launches of highly efficacious HIV, tuberculosis, or malaria vaccines would be unlikely. Estimated additional costs to launch one of each of 18 key missing products are $13.6B assuming lowest product complexity or $21.8B assuming highest complexity ($8.1B-36.6B). Over the next 5 years, total estimated costs to move current candidates through the pipeline and develop these 18 missing products would be around $4.5B (low complexity missing products) or $5.8B/year (high complexity missing products).

Conclusions: Since current annual global spending on product development is about $3B, this study suggests the annual funding gap over the next 5 years is at least $1.5-2.8B.

Link: https://gatesopenresearch.org/articles/2-23/v2

Ziemba, Elizabeth. 2005. "Public-Private Partnerships for Product Development: Financial, Scientific and Managerial Issues as Challenges to Future Success." Research Report for the World Health Organization Commission on Intellectual Property Rights, Innovation and Public Health. https://www.who.int/intellectualproperty/studies/Ziemba.pdf?ua=1.

Abstract: Not available

Link: http://www.who.int/intellectualproperty/studies/Ziemba.pdf?ua=1

** For the purposes of this review, we have established three categories to describe the state of the literature: thin, considerable, and rich.*

- *Thin: There are relatively few papers and/or there are not many recent papers and/or there are clear gaps*
- *Considerable: There are several papers and/or there are a handful of recent papers and/or there are some clear gaps*
- *Rich: There is a wealth of papers on the topic and/or papers continue to be published that address this issue area and/or there are less obvious gaps*

Scope: While many of these issues can touch a variety of sectors, this review focuses on medicines. The term medicines is used to cover the category of health technologies, including drugs, biologics (including vaccines), and diagnostic devices.

Disclaimer: The research syntheses aim to provide a concise, comprehensive overview of the current state of research on a specific topic. They seek to cover the main studies in the academic and grey literature, but are not systematic reviews capturing all published studies on a topic. As

with any research synthesis, they also reflect the judgments of the researchers. The length and detail vary by topic. Each synthesis will undergo open peer review, and be updated periodically based on feedback received on important missing studies and/or new research. Selected topics focus on national and international-level policies, while recognizing that other determinants of access operate at sub-national level. Work is ongoing on additional topics. We welcome suggestions on the current syntheses and/or on new topics to cover.

ABOUT US

The Knowledge Network on Innovation and Access to Medicines is a project of the Global Health Centre at the Graduate Institute, Geneva. The project seeks to maximize the contributions of research and analysis to producing public health needs-driven innovation and globally-equitable access to medicines.

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