Ensuring that Developing Countries have Access to New Healthcare Products: The Role of Product Development Partnerships

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Abstract

Product development partnerships (PDPs) are generating an increasing flow of health products for diseases prevalent in developing countries. Based on past experience, ensuring end-user access to these health products will present a significant challenge following the research and development process. The specific actions required to ensure access, and the time when these actions should be initiated, are becoming clearer based on the experiences to date in various PDPs. This list of activities can seem daunting, but the public health community is already learning how to spread these responsibilities between PDPs and other actors – both public and private, and international and national – such that efficiencies and local relevance are maximized.

Bridging the gap between product development and end users

For many years, there was insufficient development and supply of new health products for diseases prevalent in developing countries. Product development partnerships (PDPs) were formed in response to this market situation, which arose from a perceived lack of financial incentives and abundance of commercial risks for companies. The PDPs, as not-for-profit organizations, could bring together the public, private, academic, and philanthropic sectors to drive the necessary product development [1]. PDPs have been around for decades but, thanks to growing investments from government donors and foundations around the world, their numbers and profile have increased over the past 5 -10 years.

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An increasing number of PDPs are now facing the challenges of ensuring that end-users can access products once developed. Introduction of new tools for various indications has often been associated with a significant delay between global availability and local adoption [2-4], and the process of health technology change has presented significant challenges [5-8]. Frost and Reich (2008) have analyzed some of these challenges and proposed underlying principles for confronting them [9]. PDPs will also benefit from sharing both a forward-looking, time-sensitive menu of specific activities and a set of lessons on how these activities can help ensure access. The term "access" is used in different ways by many organizations, and for the PDPs there was a need to translate this term into an operational definition [10]. This definition can assist in defining what contributions by PDPs and other actors would have the greatest impact on ensuring timely access.

To address this issue, a diverse group of 20 organizations, including donors, NGOs, and 12 PDPs and similar initiatives, met in Geneva, Switzerland, on September 17-18 2008. The PDPs that attended are striving to develop vaccines for HIV, tuberculosis, malaria, dengue fever, meningococcal meningitis, and pneumonia, drugs for tuberculosis, malaria, sleeping sickness, and visceral leishmaniasis, microbicides for HIV, and novel insecticides. This self-convened meeting was the largest-ever gathering of a broad cross-section of PDPs and NGOs to focus on access to newly developed products.

Meeting objectives were to survey PDP experiences, best practices, and challenges in the area of access (in both the public and private sectors, and with comparisons across the access pathways for novel drugs, vaccines, and vector control), to identify the gaps and possibilities for future investigation, collaboration and coordination, and to define the role of PDPs within the overall framework of research, development, and access activities.

The meeting covered four topics: planning and introduction for implementation; manufacturing; pricing, finance, and procurement; and global regulatory pathways for new products. Shared lessons from the meeting can provide a reference for future access discussions and can inform future work. (The agenda, meeting presentations and a meeting report can be obtained from the corresponding author.)

Defining "access"

Participants agreed that, for PDPs, "access" refers to a coordinated set of activities needed to ensure that the products developed will ultimately have an equitable public health impact. Achieving that impact requires products that are available, affordable, and acceptable to end-users, and adopted into developing country health systems. The role of PDPs in addressing these four concepts has varied from doing, to facilitating, to advocating for others to take action. In order to be successful, PDPs need to collaborate closely with developing countries throughout the process from pre-clinical development to product adoption.

Although access activities vary due to differences between interventions (drugs, diagnostics, vaccines, or insecticides) and disease contexts (e.g., presence of disease-specific supporting systems or financing), there is a logical flow of potential access activities according to the stage of product or intervention development. Table 1 lists the activities that participants at the meeting identified as falling under the term "access".

Ensuring local context and ownership

Development of products is best done with a strong and clear understanding, from the outset, of the health system within which they will ultimately be used, the trade-offs that will need to be made and with consideration to the potential impact of the intervention on health systems. National decision- makers need access to sufficient and high quality local, regional, and global data and to be well-informed about the interpretation of data and experiences in other settings. The goal is for national governments to make their own evidence-informed decisions regarding use of interventions in their country. PDPs should seek to maximize country ownership of access activities at all stages, especially as decision-making becomes imminent. Involvement of developing countries in PDP activities helps in achieving this goal.

Table 1: Principal "Access" Activities

a. Pre-clinical:
- Determining stakeholder needs and eventual health system context
- Informing product profiles, including cost constraints

b. Early clinical or pre-proof of concept:
- Analyzing stakeholder perceptions and demand
- Burden of disease studies
- Profitability, return on investment (ROI) and net present value (NPV) assessments
- Refining target product profiles
- Quality control of manufacturing processes
- Identification and allocation of risk, including indemnification and insurance
- Helping to refine the regulatory framework
- Informing contractual "access" agreements with manufacturers
- Planning the fastest possible pathway through the ensuing web of access activities

c. Late clinical:
- Building awareness about the disease and the new products developed to address the disease
- Deriving strategic demand forecasts under specific delivery strategies
- Finalizing target product profiles to ensure alignment with the developing country context
- Modeling impact and cost-effectiveness
- Facilitating disease surveillance mechanisms
- Ensuring manufacturing capacity is in place
- Informing and ensuring adherence to contractual "access" agreements with manufacturers
- Understanding existing market structures and pathways for related products
- Increasing management of risk through indemnification and insurance
- Ensuring quality control of the manufacturing process
- Refining regulatory pathways
- Defining pathways for international and/or regional policy recommendations
- Beginning discussions with financing and procurement agencies
- Supporting activities to develop global, regional and local advocates
- Ensuring that countries understand their role in accelerating access to an affordable and sustainable supply of products
- Supporting the formation of country decision-making mechanisms (as described below)

d. Post-licensure:
- Ensuring implementation of essential operational research, effectiveness trials, demonstration projects, and/or Phase 4 pharmacovigilance studies
- Capacity building to facilitate ongoing pharmacovigilance
- Communicating information on the intervention
- Ensuring that countries and international agencies understand their roles in accelerating access to an affordable and sustainable supply of products
- Supporting leadership and issuance of guidelines by international technical organizations (e.g., WHO) that are mandated to advise on implementation
- Seeking sustainable financing commitments for procurement and utilization
- Serving as an expert resource to international organizations during their policy processes and countries during their decision-making and adoption processes

PDPs can support the expanded involvement of developing country manufacturers when appropriate. For example, developing country manufacturers may be able to improve future access by producing products at lower costs or adding production capacity that contributes to the development of a healthy market with multiple suppliers to help ensure adequate supply is available. As always, sufficient R&D and manufacturing capacity and rigorous regulatory oversight must be ensured.

Agreements with partners

The types of collaborations PDPs enter into with private sector partners and the terms of those agreements should seek a clear commitment to access, a clear understanding of the returns to the private sector partner, a protection of PDP investments and intellectual property (e.g., non-exclusive licensing if an industrial partner stops development), a defined target product profile, and a supply of quality products at affordable prices for countries of the developing world.

If products have significant potential for commercial markets, PDPs can establish contractual terms that allow private sector partners to pursue commercial markets, while also ensuring the investments from PDPs are translated into appropriate benefits for the public sector.

Opportunities for PDPs

PDPs have the opportunity to work with international organizations, national regulatory authorities, and industry to seek innovative regulatory and WHO pre-qualification approaches, potentially getting products to end users years earlier without foregoing rigorous product oversight. Similar opportunities exist with innovative financing mechanisms with PDPs being well positioned to navigate and help perfect these mechanisms.

PDPs can help to reinforce international strategies such as the global strategy and plan of action from the Inter-Governmental Working Group on Intellectual Property, Innovation, and Public Health.

Finally, cooperation between PDPs can increase efficiency and bolster understanding in several areas, including the structure of markets in low income countries, what contractual terms are both favorable for developing countries and fair in development, manufacturing and distribution contracts, and what metrics can be used to determine PDP success in ensuring access.

The evolving role of PDPs in ensuring access

The discussion above reflects lessons on the range of activities PDPs have undertaken when working to address "access." Each of the activities listed in Table 1 has been carried out by at least one of the PDPs. It is clear, however, that each individual PDP cannot cover all of these necessary activities alone. Rather, we see this list as a recognition of the substantial collective effort needed to ensure access to new technologies, and the focus for continued thinking on how this work is best divided among national governments, other national bodies, and existing international organizations. Within PDPs, staffing numbers and skill sets will evolve as activities and stages of product development progress. As today's investments in R&D increasingly produce important interventions in the future, it becomes ever more critical to wisely consider the range of activities that do or do not fall within the "access" remit of varying PDPs and to make sure that the entire pathway from R&D to end users is appropriately addressed.

In this new era of PDPs, we now have several more years experience and many approaches to learn from as we collaborate and strive ever more effectively towards public health goals. PDPs have a unique opportunity to share learning between organizations, which will be critical in decreasing the time between development of products and the realization of public health impact in developing countries.

Author contributions

All authors participated in the meeting where the manuscript originated and contributed to the drafting and revision of the manuscript.

Competing Interests and Funding Sources

ADB, WAW, TDM, RK, RC, TM, LAP-D, AFK, and RTM, are employed by product development partnerships, or similar not-for profit groups, and work on access-related issues.

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References

1. Moran, M: A breakthrough in R&D for neglected diseases: New ways to get the drugs we need. *PLoS Med* 2005. 2:e302.
2. Mahoney RT, Maynard JE: The introduction of new vaccines into developing countries. *Vaccine* 1999, 17:646-652.
3. Mutabingwa TK: Artemisinin-based combination therapies (ACTs): best hope for malaria treatment but inaccessible to the needy! *Acta Trop* 2005, 95:305-315.
4. Glass RI, Bresee JS, Turcios R, Fischer TK, Parashar UD, Steele AD: Rotavirus vaccines: targeting the developing world. *J Infect Dis* 2005, 192 Suppl 1:S160-166.
5. Williams HA, Durrheim D, Shretta R: The process of changing national malaria treatment policy: lessons from country-level studies. *Health Policy Plan* 2004, 19:356-370.
6. McCannon CJ, Berwick DM, Massoud MR: The science of large-scale change in global health. *Jama* 2007, 298:1937-1939.
7. Levine OS, Cherian T, Shah R, Batson, A: PneumoADIP: An example of translational research to accelerate pneumococcal vaccination in developing countries. *J Health Popul Nutr* 2004, 22:268-274.
8. Kane MA, Brooks A: New immunization initiatives and progress towards the global control of hepatitis B. *Curr Opin Infect Dis* 2002, 15:465-469.
9. Frost LJ and MR Reich. 2008. Access: How do good health technologies get to poor people in poor countries? Harvard Center for Population and Development Studies, Cambridge, MA.
10. Mahoney RT, A Krattiger, JD Clemens and R Curtiss III. 2007. The introduction of new vaccines into developing countries IV: Global Access Strategies. *Vaccine* 25(2007):4003–4011.