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Innovative Product Development Partnerships

Advancing Global Health and Economic Development Goals

Product Development Partnerships (PDPs) are non-profit organizations with mandates to research, develop and support accessibility of new health technologies that target diseases disproportionately affecting developing countries. Currently, there are over 26 PDPs developing drugs, vaccines, microbicides and diagnostics that target a range of infectious and neglected diseases, including HIV/AIDS, malaria, tuberculosis (TB), Chagas disease, dengue fever, visceral leishmaniasis (VL) and sleeping sickness. PDPs advance global health goals by accelerating the development of products that may not otherwise be developed. These products could save millions of lives and PDPs' routine collaborations with partners in developing countries as part of their research and development (R&D) activities contribute to sustainable economic development.

PDPs Fill Critical Gaps in Global Health Research and Development

PDPs are delivering on their promise to develop life-saving products for use in countries where disease burdens are highest and no viable commercial markets exist. The annual rate of new product approvals for neglected diseases increased from an average

Table 1: Biomedical Technologies Developed by PDPs

PRODUCT DEVELOPMENT PARTNERSHIP	PRODUCT
Drugs for Neglected Diseases Initiative (DNDi)	Fixed dose Artesunate/Amodiaquine (World Health Organization (WHO) prequalification, registered in 25 African countries and India) and Artesunate/Mefloquine for malaria treatment (registered in Brazil); Nifurtimox-Eflornithine Combination Therapy for stage 2 sleeping sickness (WHO Essential Medicines List and recommended in 9 countries)
Foundation for Innovative New Diagnostics (FIND)	4 TB diagnostic technologies for detection of TB and multi-drug-resistant tuberculosis (MDR-TB) (WHO prequalification)
Institute for One World Health	Paromomycin intramuscular injection to cure VL (licensed in India)
International Vaccine Initiative	Oral cholera vaccine (licensed in India)
Medicines for Malaria Venture (MMV)	Pediatric Coartem Dispersible for malaria treatment (SwissMedic approval and WHO prequalification)
PATH (encompasses numerous PDPs)	Japanese encephalitis vaccine (licensed in 9 countries); Meningitis A vaccine (WHO prequalification)

Source: Grace and Druce, 2009 and IAVI's research.

of 1.8 between 1975 and 1999 to 2.6 between 2000 and 2009. During the same time PDPs accounted for a growing share of all regulatory approvals to treat neglected diseases, from 15% to 46% (TCSDD, 2009). To date, PDPs have developed and licensed 12 products to combat malaria, sleeping sickness, cholera, Japanese encephalitis, meningitis,

PDPs provide “optimal funding allocation at all stages of research and development, in a manner best designed to maximize public health returns in the developing world.”

—WHO Expert Working Group on R&D Financing, 2009

VL and TB in low- and middle-income countries (see Table 1 on previous page). More can be expected from PDPs in the future with sustained and additional support. In 2009, PDPs had nearly 150 biopharmaceutical, diagnostic and vector control candidates in various stages of development, including 32 in late-stage clinical trials (BCG, 2009).

PDPs’ strategic collaborations with public and private sectors from developed and developing countries, combined with specialized expertise in their disease areas, accelerate the process of researching, developing and delivering life-saving products for use in developing countries. For example, the International AIDS Vaccine Initiative (IAVI) employs an integrated approach to ensuring the development of an AIDS vaccine. It has established research networks and collaborates with institutions in Africa, Asia, Europe and the United States to facilitate information-sharing. It partners with biotechnology and pharmaceutical companies with cutting-edge

technology and expertise to accelerate vaccine design and development. IAVI also collaborates with research centers in developing countries to ensure any vaccines developed are appropriate for use in regions most affected by the pandemic and advocates for greater political support for current research efforts.

Political and financial support for R&D targeting diseases of poverty has increased in recent years. In 2008, US\$ 2.96 billion was spent on neglected disease R&D: PDPs received 19.6% of total funding, with remaining funds supporting activities by non-PDP researchers and developers (53.0%), pharmaceutical and biotechnology companies (12.0%) and the US National Institutes of Health (5.4%) (G-FINDER, 2009). Although most PDPs continue to rely on funding from the Bill & Melinda Gates Foundation, the share of government funding of PDPs has grown from 7% in 2000 to 34% in 2007 (BCG, 2009), in part due to support from development donors including the United States

Agency for International Development and the Department for International Development in the United Kingdom. The current economic recession, however, has led to a reduction in commitments by some governments and other donors.

PDPs as Social Innovators: Contributions to Broader Development and Public Health Goals In Developing Countries

A recent report by the WHO Expert Working Group on R&D Financing acknowledged the high impact of PDPs on developing countries because of “their focus on developing affordable suitable products for developing country use; their routine practice of working with developing country researchers and developers; and, to varying degrees, their capacity building efforts in developing countries” (WHO, 2009).

Capacity-building in developing countries is integral to the work of PDPs. PDPs collaborate with developing country partners to advance candidates in the R&D pipeline and invest significant resources in partner countries to support and expand existing physical and systemic infrastructures in the communities in which they operate. A few examples of PDP support for capacity-building include:

- In 2006, DNDi built the Leishmaniasis Research and Treatment Centre in Ethiopia, Africa’s first clinical research facility dedicated to VL. The center is part of the Leishmaniasis East Africa Platform (LEAP), also supported by DNDi, which is a regional clinical research network comprising VL experts from Ethiopia, Kenya, Sudan and Uganda. Created in 2003, LEAP is currently assessing field effectiveness of paromomycin and evaluating other drugs for VL in Sudan, Ethiopia and Kenya. It is working with local communities to upgrade existing hospitals, clinics

Product Development Partnerships Defined

Many PDPs were established in the mid-1990s to help address the 10/90 gap – that only 10% of health research funding was targeted toward diseases that accounted for 90% of the global disease burden (GFHR, 2004). While each PDP operates differently depending on the disease area(s) of focus, they typically employ a portfolio approach to R&D to accelerate product development by pursuing multiple strategies for the same disease area. They also work in close partnership with academia, large pharmaceutical companies, the biotechnology industry and governments in developing countries. Although PDPs typically use private industry approaches to portfolio management, they focus on disease areas that lack viable commercial markets. PDPs with products in advanced stages of development have also focused additional efforts on ensuring equitable access and uptake of new products they have helped develop.

and laboratories and building up expertise of local health workers through trainings on clinical trial methodology, Good Clinical Laboratory Practice (GCLP), ethics, patient evaluation, diagnosis and follow-up (DNDi, 2010).

- IAVI has clinical research partners in countries highly affected by the pandemic, including Kenya, Zambia, Rwanda and India where the first HIV vaccine trials have been conducted in those countries (Grace and Druce, 2009). Research in Kenya has resulted in a new Ministry of Health Vaccine Subcommittee to accelerate the approval of new vaccine trials. The Uganda Virus Research Institute's HIV Vaccine Program consists of state-of-the-art laboratories, clinical space and administrative offices. It was the first program in sub-Saharan Africa to receive GCLP accreditation and was selected in 2005 to be a central laboratory in the Consortium for AIDS Vaccine Development.
- Since 2005, MMV's clinical trials of antimalarials have led to a significant improvement in R&D capacity and capability in 39 of 55 clinical research centers in over 24 malaria-endemic countries. Efforts include taking basic facilities to Good Clinical Practice (GCP) standards; supplying specialist equipment, such as molecular biology equipment, to GCP-compliant centers; and training staff in Good Laboratory Practice. MMV has used some centers to develop two new antimalarials currently awaiting regulatory approval at the European Medicines Agency, and will use others to develop novel antimalarials to address the emergence of malaria resistance recently reported in Southeast Asia. MMV has also co-piloted, with the Ugandan government, one of

PDPs Create Enabling Environments to Accelerate Product Development and Access

The Aeras Global TB Vaccine Foundation supports two initiatives led by the WHO: the Developing Countries Vaccine Regulators Network and the African Vaccine Regulatory Forum. These efforts strengthen participant countries' systems for evaluating vaccines and help regulators make informed decisions when authorizing clinical trials, evaluating registration dossiers or assessing other challenging issues regarding evaluation of vaccines (Aeras, 2010).

Laboratory capacity to properly diagnose and manage MDR-TB is an essential component of the complex response to the urgent challenges posed by MDR- and extremely drug-resistant TB. FIND has been working with the Lesotho Ministry of Health to upgrade the national TB reference laboratory. The improvements include reinforcing microscopy services, streamlining conventional culture and drug susceptibility testing, and ensuring that the new TB diagnostic methods can be effectively integrated into the country's national systems (FIND, 2010).

Since 2004, the International Partnership for Microbicides (IPM) has obtained several non-exclusive royalty-free licenses from pharmaceutical companies to develop, manufacture and distribute antiretroviral compounds as microbicides in developing countries. For example, IPM and CONRAD have an agreement with Gilead to develop tenofovir, an antiretroviral (ARV) drug, as a topical microbicide for use by women in the developing world. The agreement allows IPM and CONRAD full rights to distribute an eventual microbicide product at no or low cost. Results from a 2010 safety and effectiveness study demonstrated that a vaginal microbicide with 1% tenofovir gel offers protection against HIV. This represents the first "proof of concept" for an ARV-based microbicide (IPM, 2010).

PATH's Malaria Vaccine Initiative (MVI) is currently testing a long-awaited malaria vaccine that could avert millions of deaths, particularly among children. Along with its private sector partner GlaxoSmithKline, MVI currently collaborates with 11 clinical research centers in 7 African countries, bolstering the scientific capabilities of those countries. MVI is also working with the WHO and African countries to establish decision-making processes around vaccine use, which strengthen and improve existing systems and national capacity to achieve broader development goals (Alliance for Case Studies for Global Health, 2009).

the first private-sector distribution models for creating rural access to subsidized WHO-prequalified ACTs, specifically artemether-lumefantrine (MMV, 2010).

- The Global Alliance for TB Drug Development (TB Alliance) has assessed close to 90 sites worldwide, including sites in 16

high TB-burden countries, for their capacity to conduct registration-standard drug trials. The reviewed sites have all been provided with direct feedback on areas of strength and deficiency. The TB Alliance is developing and providing training at clinical trial sites and laboratories in Africa, Asia and Latin America identified during the clinical

capacity mapping efforts. The sites and laboratories developed as a result of the TB Alliance's moxifloxacin program will be useful for future TB clinical trials. Furthermore, through its work with researchers in developing countries, the TB Alliance is helping to build scientific expertise. For example, as part of its collaboration with the Beijing Thoracic Tumour and Tuberculosis

Research Institute, it is educating scientists on drug development (TB Alliance, 2010).

Conclusion

PDPs have evolved into an innovative organizational model to advance global health and development priorities. Investments in PDPs are impacting disease-endemic countries both as a result of the development

of new biomedical technologies to combat debilitating diseases and the partnerships forged with developing countries as part of PDPs' routine activities. With adequate political and financial support, PDPs can continue to build unique partnerships with private industry, academia, donors and developing countries to develop new health technologies and to ensure access for those who need them most.

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IAVI's policy brief series outlines key public policy issues in the research, development and eventual distribution of AIDS vaccines.

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