Commentary

Building biotechnology by design: Role of biotechnology in development

Journal of Commercial Biotechnology (2011) **17,** 4–6. doi:10.1057/jcb.2010.32;
published online 30 November 2010

Neglected diseases sicken and kill many hundreds of millions of people each year – often the very poorest in developing countries. A common characteristic of these diseases, whether they be malaria, HIV/AIDS, sleeping sickness or diarrhea, is that despite the scale of the human suffering, they represent no or very low commercial market value for pharmaceutical and biotech companies.

Without commercial incentives to develop new and improved health tools, such as medicines, the pipeline of innovative products needed to combat these diseases was either nonexistent or very slim before the 1990s.[1] Recognizing a looming global health crisis, a group of influential global health leaders designed a new type of organization in response: public–private product development partnerships (PDPs). These new organizations bridge the public and private sectors, bringing new health solutions to those most in need. These solutions include safe and innovative medicines, diagnostics, vaccines and interventions for a range of diseases including HIV/AIDS, tuberculosis, malaria, human African trypansonmiasis (sleeping sickness), chagas and others.

Taking the example of malaria, of the 250 million annual cases, 1 million die each year, most of whom are children under the age of 5 living in sub-Saharan Africa.[2] Since the first widespread use in the mid-sixteenth century of the first known antimalarial – quinine isolated from cinchona bark in 1820 – resistance has emerged to one drug after another.[3] Chloroquine was synthesized in 1934 and resistance to it spread relatively quickly following its widespread deployment. Artemisinin, first purified in 1978 by Chinese scientists from the wormwood plant, in combination with other drugs is now the treatment of choice for the vast majority of malaria cases. The early warning signs of resistance to artemisinin, however, are also beginning to appear.[4] Thus, it is critical that new safe and effective drugs are developed to ensure we have the tools to be able to continue to cure this disease.

Today's challenges encountered to eradicate malaria are numerous: resistance, lack of child-friendly treatments, no vaccines and limited access to affordable medicines. Medicines for Malaria Venture (MMV) was designed as a virtual PDP organization to help address some of these issues.[5] By serving as the interface between the public and private sectors MMV orchestrates research and development (R&D) and access work to provide safe, efficacious and affordable antimalarial drugs where they are most needed.

MMV was founded in November 1999 in Geneva, Switzerland, with the support of the World Health Organization (WHO), and the International Federation of Pharmaceutical Manufacturers & Associations. Seed funding (US$4 million) was provided from the Swiss Government, UK

Department for International Development, the Government of the Netherlands, The World Bank and the Rockefeller Foundation. Currently 42 employees work for MMV.

MMV is now managing the largest portfolio of antimalarial medicines in history, with over 50 projects in different stages of development (discovery, preclinical, clinical and registration stages) or approved for treatment (for example Coartem® Dispersible, a child-friendly artemisinin combination therapy developed in partnership with Novartis).[5]

The MMV business model became a success thanks to (a) substantial and continuous funding (more than US$515 million) from 14 donors that include the Bill & Melinda Gates Foundation and several governments, (b) significant in-kind contributions from our international pharmaceutical partners (for every dollar out, MMV receives at least $1.1–$1.3 equivalent back) and (c) research collaborations with academic institutions throughout the world interested in socially responsible projects and dissemination of their know-how or inventions for greater public good.

MMV's philosophy is to spend wisely and share our discoveries. Indeed, all our Intellectual Property and much of our know-how and knowledge are contributed to the Pool for Open Innovation against Neglected Tropical Diseases,[6] and can be accessed by interested parties from/for developing countries. The MMV business model in the field of malaria contributes to a better world and was designed to have a significant impact on the malaria burden.

There are still three major challenges faced by PDPs such as MMV:

1. *Dependence on philanthropic funds*: In order to function as designed, PDPs must secure continuous and significant funding. Continuity is particularly important for PDPs, such as MMV, involved in R&D of new health tools owing to the timelines involved in taking an idea from conception to fruition. In MMV's case this requires donors with both patience and sophistication. Several initiatives (internationally coordinated) are now underway to permit sustained funding of global health diseases, which follow the pioneering paths of Bill & Melinda Gates, Warren Buffet and other philanthropists, as well as foundations such as the Rockefeller and Welcome Trust.

2. *Maximizing access to medicines*: Developing medicines registered under stringent regulatory authorities is inadequate if they do not get to the people who need them most. In 2006, MMV started addressing some of these issues and has since built a small team dedicated to the provision of information, preliminary analysis, tools and data for improving the system dynamics of access and delivery of antimalarial drugs. From the country/district level, to the most remote places, MMV has been involved in driving several pilot studies. One such pilot study led by MMV and the Ugandan Ministry of Health showed that an initiative to subsidize the cost of artemisinin in the private sector could successfully increase stocks and affordability. The study results were so compelling that the subsidy mechanism will be extended to other countries to increase patient's access to medicines.

3. *Alliance management*: The PDP model is designed as a connector or bridge between private and public sectors. Thus, MMV acts as a virtual drug development organization, coordinating the work from basic science to the delivery of an approved drug. The participating parties in the fight against malaria have divergent interests, and the complexity of the network is very significant. MMV works to keep all the interested parties committed, participative and open in order to deliver high performance. Although its mandate as an International Non-governmental Organization is clear, MMV must effectively manage the sometimes contradictory objectives of its partner's interests:

commercial versus socially responsible; return on investment versus global health impact; country level versus global health policy for eradication.

4. *Children-friendly treatments:* Eighty-five per cent of those who die from malaria are children under the age of 5. Yet the traditional process for drug development is to first develop an adult formulation, with pediatric formulations considered sometimes years after the initial adult launch, if at all. High costs for clinical trials, exceptional needs for safety for young children and sometimes complex interactions with drugs mean that developing safe and effective medicines for children represents a particularly high hurdle. As a mission-driven organization, MMV is committed to developing affordable child-friendly antimalarials, thereby improving their acceptability and compliance. MMV is now working closely with the WHO Essential Medicines for Children program and its 'make medicines child size' campaign to expedite policy changes relating to pediatric treatments, by relaying timely information on their development.

In conclusion, MMV's contributions will be insignificant if they are not fully integrated within the global health community toward the ultimate goal of malaria eradication. Bringing together the private and public sectors, and philanthropists to execute the PDP business model has proven to be a success – and one that can be extended to other burning global issues.

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