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Medicines for Malaria Venture

A new public/private approach to develop affordable medicines

Von Robert G. Ridley

The infectious disease burden inflicted on the developing world by tropical diseases continues to exact a huge price both in human suffering and in contributing to poverty and underdevelopment. Neither the industry, through the existing market, nor the public sector, through its traditional approaches, can address this problem alone. Mechanisms that enable both industry and the public sector to combine resources and expertise are required to meet this pressing public health need. The recently established Medicines for Malaria Venture (MMV) is an example of such a new approach.

The case of malaria is particularly acute: Because of scientific and technical obstacles, vaccines are non-existent and, due to the growth of resistance, drugs are becoming inadequate. New products are desperately needed, especially affordable drugs to treat uncomplicated disease. However, the increased costs of developing and registering pharmaceutical products, coupled with the prospect of inadequate commercial returns, has resulted in the withdrawal of the majority of research-based pharmaceutical companies from research and development (R&D) investment in tropical diseases, especially from discovery research activities. The public sector has maintained basic science funding, but in general lacks the expertise, mechanisms and resources to discover, develop, register and commercialise new products. If the status quo continues, the outlook for the control of many of the world's major diseases, as we approach the new millennium, looks bleak.

The Medicines for Malaria Venture (MMV) (1), launched as an independent Swiss Foundation in November 1999, represents a new approach to tackling the discovery, development and commercialisation of badly needed drugs for diseases where there is insufficient market incentive to support and justify a competitive industry involvement. It is based upon a partnership that has been established between the research-based pharmaceutical industry and the public sector (2) and its establishment was the result of discussions and negotiations over several years that included representatives from both sectors (3). The process was greatly facilitated by the establishment by the World Health Organisation (WHO) of the Roll

Back Malaria Project (4) and of a series of regular round table meetings between WHO and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA). MMV will operate under the umbrella of Roll Back Malaria.

MMV's mission and how it can be accomplished

The goal of MMV is to fund, support and manage a portfolio of drug discovery and development projects that can lead to the registration and commercialisation of one new product every five years. We believe that this is the appropriate frequency of introduction of new antimalarial drugs that will make a sustainable difference to malaria control, given the rate of resistance development and other issues that can limit a drug's acceptability. The products of the venture are targeted at low-income populations in disease endemic countries. This provides an additional challenge as not only must new drugs be discovered and developed, but there is a necessity to ensure that they are appropriate and affordable, as discussed below.

MMV operates as a small not-for-profit business under the supervision of a Governing Board and with a management team that has the operational independence to make decisions as it sees fit. It will report back annually to its partners and stakeholders. A diagrammatic presentation of MMV's governance structure is shown in Figure 1. It is important to draw the operational distinction that MMV will financially support projects up to the stage of product registration and will seek partners for commercialisation, but that MMV 'itself' will not produce and commercialise new products. Operating through its business paradigm however, it will seek an appropriate share of Intellectual Property Rights for discoveries generated through its research and will use this as the basis for negotiating the outlicensing of products that it develops to private sector companies.

Ensuring the affordability of the antimalarial drugs in developing countries will be a key goal of these outlicensing negotiations, while recognising that the commercialising partner, who is still taking some commercial and financial risk, needs to earn some profit. The key to MMV's ability to promote affordability in these negotiations lies in the fact that because MMV has taken on a major burden of the R&D costs, and substantially reduced the commercialising company's risk, this does not need to be figured in to the price and the return calculations of the commercialising company. This is illustrated in Figure 2, which shows a graph indicating the standard cost and return figures associated with a new product and superimposes on to this the effect of MMV's subsidising of the R&D costs.

A key component of MMV's success will hinge around its ability in outlicensing negotiations to maintain a clear focus on the desired outcome of affordability but to retain flexibility in the contractual mechanisms by which it reaches this desired outcome. Experience shows that each negotiation and each commercial partnership will be different with different companies having different priorities. For example the negotiations are likely to differ significantly depending on whether the commercial partner is a large multinational, a small manufacturer in a developing country or a start-up biotech company. They will also differ depending on the degree of

investment and time contributed, and risk taken, by the commercial partner on the project e.g. whether it has entered the partnership early in the discovery phase or late in the development phase.

Before MMV can begin such outlicensing negotiations however it must first deliver projects and drugs worthy of registration and commercialisation. This is a very complex 'upstream' task, in which failure is a more common outcome than success, but where success is a prerequisite before any drugs can be made available. Nevertheless it rarely generates as much discussion or attracts as much scrutiny as the 'downstream' issues of IPR and pricing policy in the context of a public private partnership. What is clear even at this stage is that MMV's R&D activities and its willingness to garner and use IPR (so called push mechanisms) will put significant downward pressure on the pricing of drugs in which has a partnership stake.

To achieve its goal of one new project every five years MMV must build up a portfolio of projects in recognition of the fact that each project individually has a significant chance of failure (drug R&D is a risky business). Projects will be operated and managed along industrial paradigms and funded accordingly. It is envisaged that the majority of projects will run as partnerships between public sector agencies (academia, governmental research organisations) and industry, so that the expertise existing in both sectors can be harnessed. However, stand alone projects involving only public sector organisations or only private sector organisations (e.g. Biotech companies) are also possible. It is envisaged the majority of the cash resources to support MMV will come from the public sector and philanthropic foundations, supplemented by significant support and resources (gifts in kind) provided by the industrial partners. It has been estimated that an adequate portfolio of projects will ultimately require funding levels of up to $30 million per year (5). If MMV is successful and realises its ambition of one new product every five years this means that the cost of each new antimalarial to MMV will be about $150 M.

This is a lot of money, but it still falls short of the industry estimates of $500M per new product on the market. The reasons for this are twofold. First, MMV is sharing the full cost of its R&D. Project partners, especially the industrial partners, subsidise costs through gifts in kind and access to high technology infrastructure, resources and services such as high throughput screening, worth many millions of dollars per year. Secondly, much of the costs of modern medicine are associated with the high cost of clinical trials. Because malaria chemotherapy trials are relatively straightforward and because of a vast public sector network available to assist with these trials, these costs are likely to be lower than the industry average.

Current status of MMV

Up until now, MMV has operated from within TDR, the UNDP/ WORLD BANK/ WHO Special Programme for Research and Training in Tropical Diseases, in close proximity to the Roll Back Malaria secretariat. However, the Board is now established under the chairpersonship of Dame

Bridget Ogilvie and a Chief Executive Officer has been appointed, who is about to take up office and create a small management team. MMV will therefore soon establish new offices in Geneva.

The management team will take over the administration of three major projects selected for funding from a 1999 call for project proposals. The process of project selection in 1999 confirmed the viability of MMV and the willingness of pharmaceutical companies to engage in this venture. From 101 applications from 27 countries, many involving private sector partners, both large and small, three main projects were selected for funding at a cost of $4 M per year. Each of these discovery stage projects have a major pharmaceutical company as partner (Glaxo Wellcome, Hoffmann-La Roche, SmithKline Beecham) and in each case intellectual property rights to any compound selected for clinical development, registration and comercialisation will reside with MMV. At a stroke, the level of industry involvement in malaria drug R&D has been increased several-fold and the fruits of this involvement are clearly primarily directed towards meeting developing country public health needs rather than commercial needs.

The funding requirements for MMV to deliver on its Goal are significant. However, initial fundraising activities and continued support from MMV's partners (see footnote 2) has been very encouraging, with pledges of $15 Million for the years 1999 to 2000. The recent contribution of the Bill and Melinda Gates Foundation of $25 M (at $5 M per year) over the next 5 years has considerably strengthened the financial sustainability of MMV and enabled MMV to initiate a second round of project selection. It is anticipated that at least one of these projects will be a later stage development project rather than an early stage discovery project, increasing MMV's chances of making an early impact on public health. However, further partners and stakeholders are required to guarantee MMV's ability to deliver on its mission of registering one new drug every five years.

MMV in context - Push and Pull mechanisms

There is a growing body of literature discussing how to incentivise industry engagement in product R&D for the neglected infectious diseases. MMV is an example of a so-called 'push' mechanism whereby it focuses its funding on moving specific R&D projects forward, thus adding value to the projects and reducing both the cost and the risk sufficiently to justify a company's commercial engagement in the product. Another type of mechanism frequently outlined are so-called 'pull' mechanisms by which the purchase of products are facilitated in some way by the public sector, thus ensuring a sufficiently large market to induce industry to enter. At the moment there are few examples of effective 'pull' mechanisms in existence but several interesting ideas, e.g. purchase funds (6), are being promoted. Both mechanisms are complementary in their goals and in their applications and both should be encouraged as anything that can be done to ensure the availability of new products and their accessibility to those that need them is to be welcomed. Ultimately, the most cost-effective use of public funds will probably reside in a combination of both push and pull mechanisms.

MMV in context - Partnerships

Malaria is a huge problem, with over 1 million deaths per year and 300 to 500 milion clinical cases set against a backdrop of poverty and underdevelopment. No one organisation can tackle this problem or those of other inter-related neglected infectious disease. It requires a broad partnership of activities by multiple players and stakeholders, including the public sector, philanthropic sector, private sector and civil society, such as is being attempted through Roll Back Malaria. Through endeavouring to secure the availability of effective antimalarial treatments into the future, MMV, with the assistance of its partners and stakeholders, hopes to make a useful contribution to this global effort.

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Sources

1. Information on the venture and some background articles can be found on www.mmv.org

2. Partners include World Health Organisation, World Bank, Global Forum for Health Research, Bill and Melinda Gates Foundation, Rockefeller Foundation, UK Department for International Development, Netherlands Minister for Development Cooperation, Swiss Agency for Development and Cooperation, International Federation of Pharmaceutical Manufacturers Associations.

3. The background to the establishment of MMV has been outlined in a paper by Robert G. Ridley, Win E. Gutteridge and Louis J. Currat presented at 3rd Global Forum for Health Research in Geneva, June 1999 entitled 'Medicines for Malaria Venture (MMV): A case study of the establishment of a Public Sector / Private Sector Partnership'. The paper can be accessed through the MMV website (www.mmv.org).

4. See following web site for information: www.rbm.who.int

5. This figure is based on the costs of individual projects, taking into account the value of 'gifts in kind' and infrastructure support from industry and public sector project partners, and their likelihood of progression through the different phases of discovery and development. It needs to be realised that in drug discovery and development there is a high attrition rate i.e. many projects will fail. The figures have been validated by the Boston Consulting Group who undertook a costing and benchmarking exercise during the preparation of MMV's Business Plan, funded through the Rockefeller Foundation.

6. Jeffrey Sachs, Economist, August 14th, 1999 pp17-20.

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