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Abstract

Many new Product Development Partnerships (PDPs) have recently been formed with the sole objective of developing drugs for neglected diseases with a high prevalence in the developing world. Medicines for Malaria Venture (MMV) is a PDP that was established in 1999 to develop new effective drugs for malaria. With an initial mission to “discover” and “develop” drugs, in 2006, MMV took on the additional challenge of “delivery” of its products. This presents the organization with a series of new challenges considering the market for these drugs does not function properly. This paper identifies the main issues to be addressed in order to ensure the uptake of anti-malarial drugs and examines MMV’s role as a public private partnership in tackling these issues. It then uses stylized models to understand the need and potential benefits from MMV's involvement in these areas. This research provides MMV with the tools to develop a clear strategy to approach their role in access and delivery of anti-malarial drugs to patients in endemic countries.

Keywords: Malaria, Global Health Supply Chains, Product Development Partnerships, Access to Medicines, Medicines for Malaria Venture, Price-Setting Newsboy, Boundary of NGO

1. Introduction

Despite accounting for over 80% of the global disease burden, neglected diseases of the developing world represent a very small portion of pharmaceutical research and development (R&D). This is due in part to the high cost of pharmaceutical R&D and the limited ability of for-profit companies to recover investments on new products which are targeted primarily for poor patients. The lack of availability of medicines to people in developing countries results in huge global economic expense and loss of human life. The discovery and development of drugs for neglected diseases is a global public good that has been undersupplied by the private pharmaceutical sector (Kremer and Glennerster 2004).

Financed by an influx of new public and philanthropic funds directed towards neglected disease R&D, many new Product Development Partnerships (PDPs) have been formed with the sole objective of developing drugs for these diseases. PDPs are based on a partnership model involving private pharmaceutical companies, public institutions and private philanthropic organizations. Medicines for Malaria Venture (MMV), TB Alliance, Drugs for Neglected Diseases Initiative (DNDi) and Institute for One World Health are examples of the main PDPs that have been created in the last several years. This paper focuses on MMV, a PDP developing high quality medicines for malaria.

Upon the successful development of a product to treat malaria, MMV faces a series of practical and operational challenges to ensure the effective delivery of its product at affordable prices. Uptake of their products by poor patients – the primary target of its work – faces a variety of downstream hurdles. MMV needs to build decision approaches and operational plans for many of these downstream activities. It has to decide in which downstream activities it should invest to maximize the uptake of their products. Since the PDP model strongly hinges on partner pharmaceutical companies or academic institutions developing the products, MMV also needed to make commercial agreements with its development partners stipulating conditions to ensure there was an adequate supply in the market and that the product reached the target population.

Taking into account that both public and private sector access to essential medicines, including those for malaria, is fraught with challenges in most developing countries, and that existing theoretical frameworks are not sufficient to provide

answers to the problems of access and delivery in the context of market failure, this paper provides MMV with a method to think about what areas of delivery to get involved in. The paper takes the following form. Section 2 gives an overview of the malaria problem, the creation of MMV, and the challenges of ensuring widespread access to its products. Taking the case of Uganda, section 3 outlines the main challenges to the uptake of treatments under the headings of acceptance, affordability and availability. Section 4 looks at the role of MMV in access and delivery, considering its position as a PDP. Section 5 analyzes the issue of pricing, and its impact on demand and investment of MMV pharma partners to respond to the likely uptake of products. It also examines the role of demand forecasting in helping manufacturers understand the likely curve of the evolving market for medicines.

2. Malaria and MMV

Half of the world's population - 3.3 billion people living in 109 countries - are at risk from malaria (Roll Back Malaria 2009). Approximately 250 million cases of malaria are reported, and over 800,000 people die from the disease each year. Most of these deaths are children under five years old. Chloroquine, the long used treatment for malaria, has been rendered ineffective in most parts of the world. Over the past 20 years the most lethal form of the malaria parasite, p.falciparum has developed resistance to it.

Artemisinin, derived from a Chinese shrub, is a highly effective remedy to combat malaria and one to which the malaria-causing parasite had not yet developed resistance. However, experts fear that the use of Artemisinin as a single drug over long periods of time will eventually lead to drug resistance, as occurred with chloroquine (The Economist, 2007). To combat this problem the World Health Organization (WHO) recommended the use and development of drug combination treatments known as Artemisinin Combination Therapy (ACT), and on April 25, 2002 added Coartem® to its list of essential medicines.

MMV was created in 1999 to focus on developing new ACT medicines for malaria. Up to that point, research to develop medicines for malaria had been very sluggish. Only one new anti-malarial drug was developed in the decades leading up to the turn of the millennium. Faced with no new investments in malaria drug R&D, the significant burden of malaria in poor countries, and the potential for parasite

resistance against the only available drug, a number of country governments, philanthropic foundations and multilateral institutions established MMV as a public-private product development partnership. The goal was to leverage the enormous capacity and expertise of private pharmaceutical companies and academic research institutions in drug development while minimizing their financial investment in the process. Over the 10 years of its existence, MMV has developed a healthy pipeline of over 40 malaria medicines in different stages of development. Its first product, a dispersible child-friendly version of Coartem ® was launched in 2009 and 2 others from different manufacturers will be ready to launch within the next 5 years. Experience of Coartem® (the anti-malarial developed by Novartis), showed that development and approval of drugs is not sufficient. Ensuring the uptake of these drugs is a real problem in malaria endemic countries due to a variety of downstream factors. Figure 1 provides some evidence of this problem.

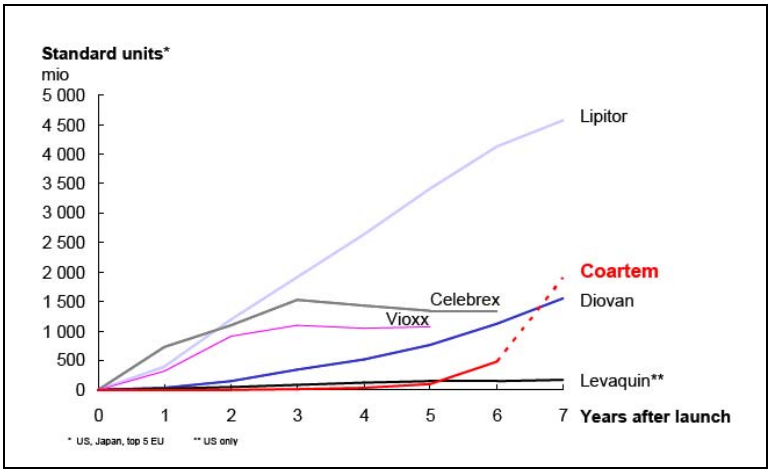

Figure 1: Downstream bottlenecks led to poor uptake of Coartem®, Novartis' anti-malarial drug (Source: Spar and Delacey 2006).

MMV's original objective focused only on discovery and development of malaria drugs. MMV has now expanded beyond its core functions of drug discovery and development to include access and delivery as a means of ensuring that people in endemic countries have access to the new products. This expanded mission raises entirely new challenges for MMV, as it now seeks to ensure that its products reach the target populations. Unlike discovery and development, access and delivery are areas in which MMV currently does not have an institutional comparative advantage. Its comparative advantage in this area comes from better understanding of the product and its launch timelines; not from better understanding of the market or prior

experience of having dealt with these issues. The area of access and delivery require a deep understanding of the issues involved before deciding on a strategy to deal with these challenges.

Sections 3 and 4 give an overview of the key issues involved in access and delivery of malaria treatments. They also introduce suggestions as to what MMV's role should be, as a PDP, in ensuring the uptake of products in their portfolio.

3. Challenges to the uptake of anti-malarial drugs

Ensuring that the target population has access to effective malaria treatment is a complex process and is dependent on multiple factors related to acceptability, affordability and availability (see figure 2). In order to achieve the objective of contributing to reduced malaria mortality and morbidity, MMV-supported products need to be available immediately when needed, at the right price, at the right place and with the right information (MMV). We analyze the challenges to achieving better acceptance, affordability, and availability of MMV products in order that MMV can prioritize its strategic role in the area of access.

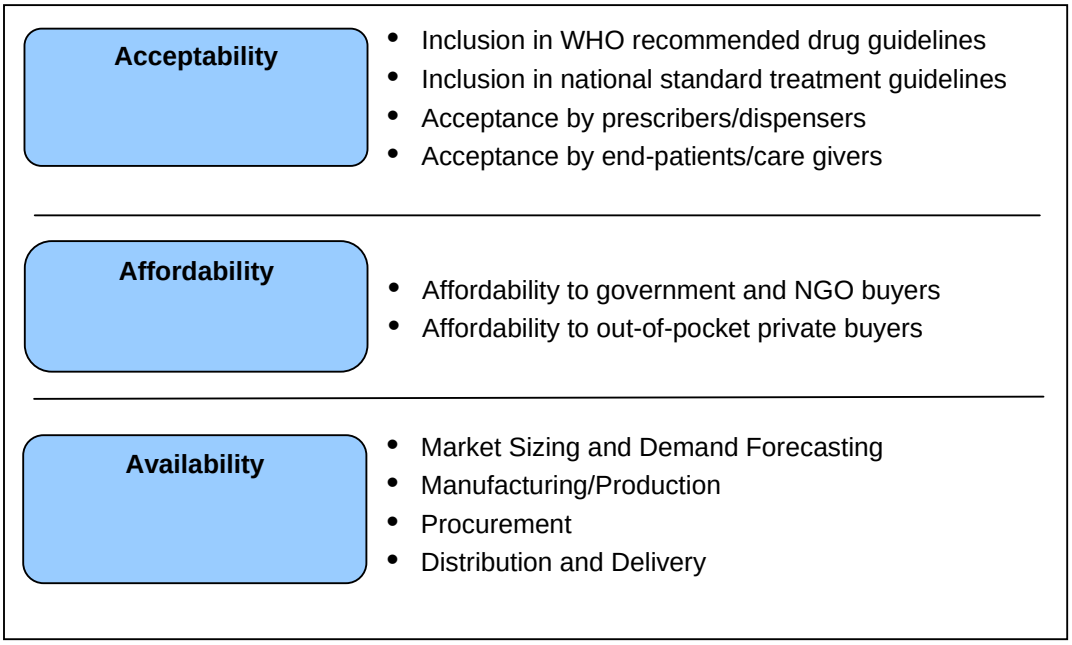

Figure 2: Factors affecting uptake of malaria treatment

3.1 Acceptability

In terms of MMV product roll-out, the first priority of gaining acceptability is to secure the authorization of a stringent regulatory authority (SRA) to market the product, and then to secure WHO Prequalification (PQ). Without this acceptance,

MMV and its pharma partners will not introduce their malaria products into the marketplace. After SRA and WHO PQ, the products must be registered in endemic countries for use in the public and private sectors. In addition, to have maximum impact, the products must be accepted for public sector use by national committees of experts and key opinion leaders who recommend treatments for national malaria control programs.

In terms of *acceptability*, assuming that the treatment receives national and international registration approval, serious challenges still remain to ensure acceptance by prescribers and patients. In most endemic countries, for a sizeable portion of the population, the first treatment for malaria is self treatment. A strong effort is required to inform and educate care-givers as well as the end users about the treatments in MMV's portfolio.

3.2 Affordability

A major obstacle to access for MMV's products is *affordability*. Although a large number of patients' access malaria treatment in the private sector, the price of high quality malaria treatments like ACTs is prohibitively high, due to the relatively high manufacturing costs relative to older, less effective drugs such as Chloroquine (CQ) and sulfadoxine-pyrimethamine (SP). This severely limits the penetration of ACTs and patients/care-givers resort to less expensive but ineffective treatment with CQ,SP, or sub-standard mono-therapies.. Retail prices for ACTs in the private sector are 10 to 40 times higher compared to CQ and SP. The structure of the private distribution channel and markups further exacerbate the affordability gap of high quality anti-malarial treatment and continue to be key uptake limiting factors.

Many of the drugs in the MMV portfolio are new ACTs and their cost structure will be very similar to existing ACTs in the market. Even if the manufacturers sell these ACTs at cost, they risk being unaffordable to a large majority of patients. It is thus important for MMV and its partners to know to what extent the high prices are driven by high manufacturer wholesale prices or by profit margins of channel intermediaries (figure 3).

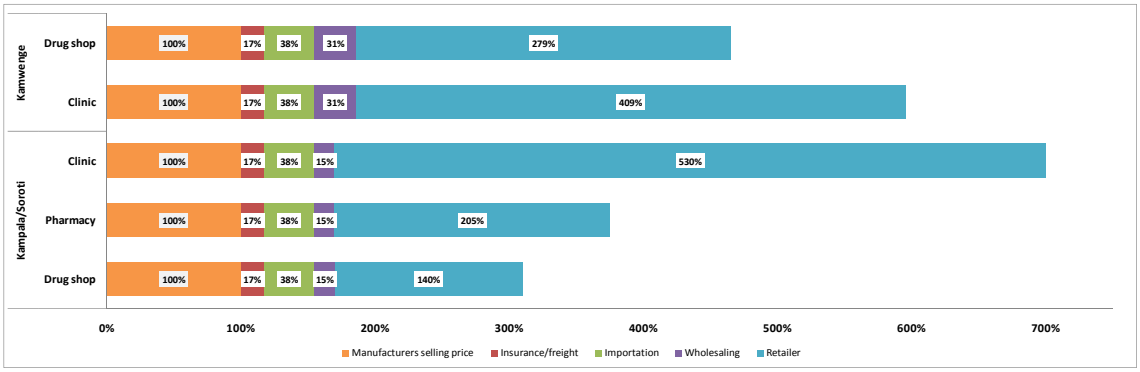

Figure 3: Prices and margins of different distribution chain players for a typical imported drug in Uganda (Source: MMV 2007)

Using the example of Uganda, figure 3 shows the build-up of price to the end patient based on manufacturer price, insurance and freight, import duties and overheads, wholesale markup and retail markup in an urban (Kampala/Soroti) and a rural district (Kamwenge). A large part of the end patient retail price is attributed to the margin of the retailer which is highest for private clinics. This shows that while ensuring manufacturer price remains low is critical (if markups are on a percentage basis a high input price means larger absolute markups) understanding retail competition and what drives high retail profit margins becomes critical for improving access. For instance, private clinics could be charging high markups on drug dispensing in lieu of a consultation fee because the willingness to pay for prescriber consultation fee may be lower.

3.3 Availability

Drugs may also be provided free in government-run clinics. However *availability* is still a major issue. Some socio-economic factors impacting on this include: the distance of the facility from the patient, lack of availability of transport and poor infrastructure. In some families, more than one person could be sick at a time, rendering long trips to seek treatment virtually impossible (Stapleton, Yadav, and Van Wassenhove, 2009).

The private sector plays an important role in the provision of drugs close to people's homes because of better accessibility, shorter waiting times, and higher reliability of the drug being available (Goodman et al 2007). In many countries such as Uganda, Nigeria, Tanzania, the private sector is the most important source of anti-malarial treatments across all income segments of the population (see figure 4). This

sector for drugs includes registered pharmacies, licensed drug shops, general stores and in some cases small kiosks or street vendors. However, as illustrated in table 1, registered pharmacies are typically more concentrated in capital cities. Drug shops and private clinics are the more common source for anti-malarial drugs in rural and per-urban areas.

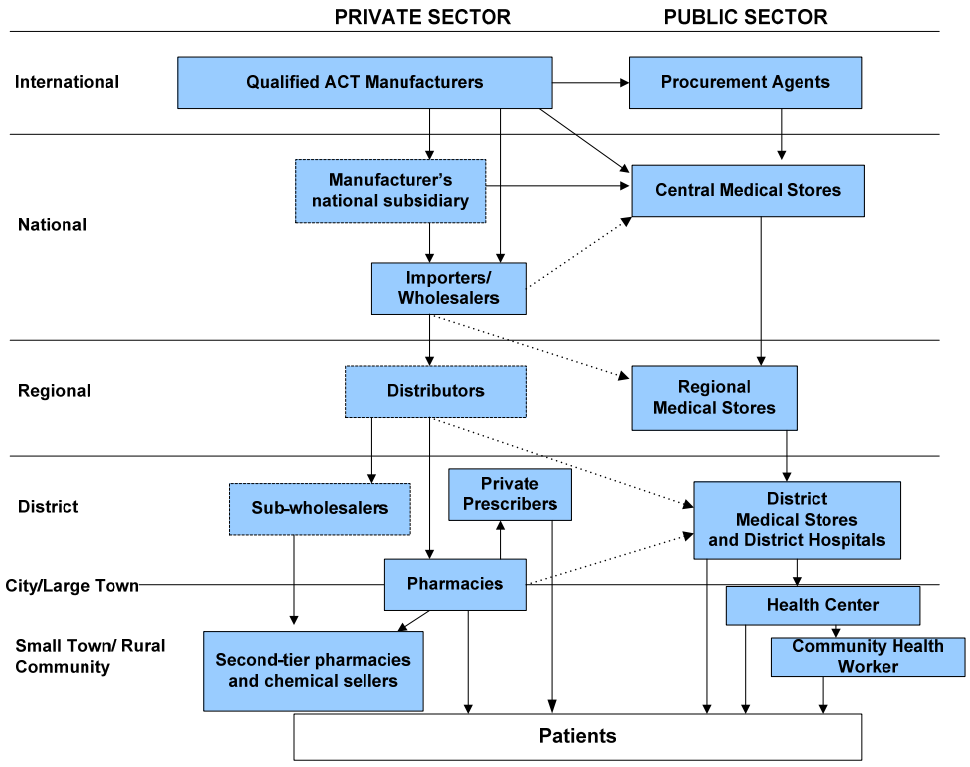

Figure 4: Distribution chain for anti-malarials

	Public and not-for-profit sector				Private sector					
	Public facilities		NGO/ mission facilities		Pharmacies		Drug Shops		Clinics	
	#	Pop. per outlet	#	Pop. per outlet	#	Pop. per outlet	#	Pop. per outlet	#	Pop. per outlet
Uganda	2,100	13,333	485	57,732	328	85,366	3,850	7,273	2,700	10,370
Kampala	39	51,282	39	51,282	168	11,905	638	3,135	1,640	1,220

Table 1: Number of different types of outlets selling anti-malarials in Uganda and Kampala (Source: MMV 2007)

MMV's policy is to work with public and private sector distribution channels. In the long-run, MMV's products should be distributed through each of the two sectors but in the short run a prioritization of channels for MMV's activities could be

required. If mortality and morbidity reduction is the target, MMV should ensure that its products are available where patients seek treatment; in public health clinics and private outlets in as long as quality can be ensured. However, currently there is very little knowledge of the private sector market and hence MMV's activities on improving market understanding should focus on the private market.

4. What is MMV's role as a public private partnership?

It is not possible for MMV alone to address the issues outlined in section 3. It would not be economically or strategically right for MMV to attempt to do so, nor would it fit with MMV's business model of working in a partnership. A large numbers of actors, such as Ministries of Health of malaria endemic countries, the World Health Organization (WHO), private industry, global and national drug regulatory authorities, NGOs, and donor organizations need to be involved to accomplish many of these access enhancing activities. As MMV moves ahead with its access and delivery objectives however, its ability to understand distribution channels for its products and to manage its relationships with multiple actors directly or indirectly involved in the supply chain becomes increasingly important.

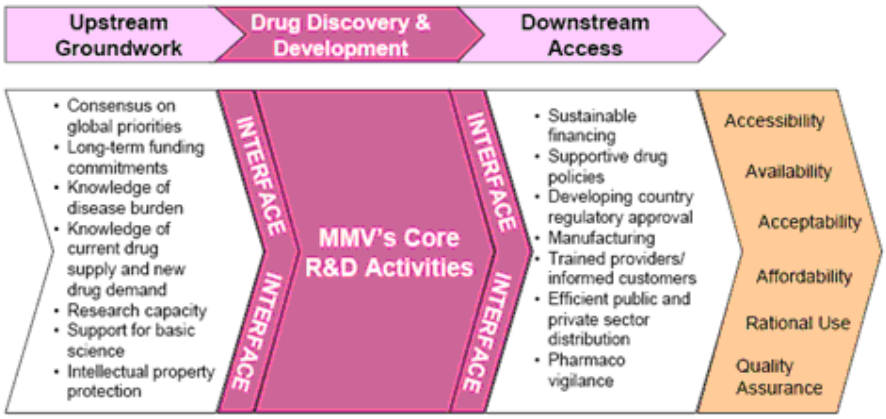

Figure 5: MMV's Core Activities and Organizational Interfaces (Source: MMV)

MMV operates like a 'virtual company'. Managing an organization such as MMV requires selecting partners, managing partner interfaces and writing and implementing multiple contracts to effectively cover for all of the upstream and downstream activities in MMV's mandate. Figure 5 details these activities. MMV already possesses the expertise for contracting and managing interfaces involving R&D. The concept of contracting in complex inputs based on strategic priorities and needs is not unusual for for MMV or other PDPs. Contracting with development

partners or other external partners for activities related to access is an extension of this process but can present challenges based on different needs relative to R&D contracting. Issues such as how to set price or guarantee capacity investment by the development partners involve complex negotiations. Setting price and capacity is contingent on both parties knowing in advance the technical details of production, marketing and distribution costs. A further problem relates to the issue of public and private goods.

4.1 Global public goods and private goods

MMV is a public private partnership which was created to supply *global public goods* (i.e. drugs for malaria) (Kremer, 2006). A *public good* is one that is public in consumption. Their provision may require collective action and their benefits cannot be privately appropriated. The development of malaria drugs is a *global public good* as the benefits from reducing malaria burden or eliminating malaria accrue globally because of reduced transmission across countries. The collective incentive is higher than each individual country's incentive. MMV's decision problem is to think about whether some of the potential activities it could carry out under access and delivery could be considered for *global public goods.*

From an efficiency-maximizing perspective MMV could potentially play a role in bringing economies of scope for all its product development partners by engaging in activities such as drug registration or advocacy to ensure higher adoption of a selection of essential drugs. However, each of the private partners will have a competing product and thus MMV's role should ideally be limited to those activities which are *global public goods*.

Although markets for malaria medicines are *private goods,* the institution of market itself is a *public good* (Kremer 2006), and the institution of global market is a *global public good*. The more buying and selling agents participate in the market, the more competitive and efficient the market is likely to be. Interventions that address this issue are also *public goods*. Similarly, the development of a solid knowledge base on what public policy, structural and regulatory changes work best in making markets for malaria medicines more efficient in endemic countries is also a *global public good*.

MMV's strategic question of what activities in access and delivery to undertake and what activities to rely on external partners to successfully execute is

related to the question of the boundary of the firm (Williamson 1975 and 1985). We focus on transaction cost theory to analyze this question. We find that it is not sufficient to cover all the issues involved and suggest an alternative framework of analysis.

4.2 Transaction cost theory: The dilemma of market failure

In transaction cost theory Williamson (1985) categorizes transaction costs associated with externally contracted functions into: *information costs*, i.e. cost of effort involved in seeking information on a potential partner to carry out this role; *bargaining costs*, i.e. cost of effort involved in negotiating and establishing the contracts with external partners and *enforcement costs*, i.e. costs to enforce and control performance, resolve conflicts and renegotiate contracts. In addition there are uncertainty related costs e.g. not knowing the future resources required to carry out some of these activities internally. The existing theoretical frameworks for defining the boundary of the firm (Williamson 1975 and 1985) are based on the premise of a functioning market and government and thus may not apply well in the current context.

The lack of access to effective malaria medicines often results from a failure of market forces and structures that could facilitate access. In other instances, it results from a failure of the state to fulfill its responsibilities to provide certain services to its population (government failure). Very often, however, it is a combination of the two with little ability to separate the nature of the failure. Weak market structures, uncertainty in demand, bottlenecks in supply, poor procurement systems, unreliable financing and weak or non-existent health systems are examples of factors contributing to lack of access. Transaction cost theory alone is not sufficient to define firm boundaries in a situation of market and government failure, such as that faced by MMV. We therefore develop a framework (table 2) which categorizes the activities that MMV could pursue as part of their access and delivery mandate and those that could be undertaken by their partners.

Activity	Needs of MMV Developing Partner	Strength/ competence of MMV relative to external partners	High Transaction cost of working with external partners	Global Public Good
Availability				
• Market Sizing and Demand Forecasting	✓		✓	✓
• Manufacturing/Production				
• Procurement				
• Distribution and Delivery	✓		✓	✓[1]
Affordability				
• Affordability to government and NGO buyers				✓[1]
• Affordability to out-of-pocket private buyers	✓			✓[1]
Acceptability				
• Inclusion in WHO recommended drug guidelines	✓	✓	✓	
• Inclusion in national standard treatment guidelines	✓	✓	✓	
• Acceptance by prescribers/dispensers			✓	
• Acceptance by end-patients/care givers			✓	

[1] Even though the activity itself may not directly create a public good, creating knowledge (and thus operational pilots to improve that knowledge) on how to best carry out the activity is a global public good.

Table 2: Access activities matrix for MMV

We draw on elements of transaction cost theory, core competency theory, global public goods creation and needs of MMV's pharmaceutical partners to help MMV select the activities within the access and delivery space it should focus on. In Table 2 we summarize the potential activities that MMV's Access group could focus on. We then validate for each of these activities whether it is perceived as a need by MMV's partners, the relative strength of MMV in engaging in it, the transaction cost of relying on external partners for it, and whether or not the activity creates a global

public good. This analysis is based on the interviews with MMV team, MMV's stakeholders and external partners working in this area carried between Feb 2007 and Oct 2007. For instance, ensuring that products in MMV's portfolio are included in WHO recommended drug guidelines or national drugs guidelines is needed by MMV's partners, MMV's access group has a relative strength in this activity and the transaction costs of relying on an external partner for carrying out this activity would be extremely high. Similarly, ensuring the distribution and delivery of MMV's products in the target markets is a perceived need by its partners and the transaction costs of working with an external partner will be extremely high as knowledge about the distribution chains in low and middle income countries is typically highly tacit and not easily codifiable. Also, creating such knowledge is clearly a global public good as it would improve the efficiency of the market. From table 2, we find that MMV should initially focus its access activities on market sizing and demand forecasting, developing better understanding of the distribution system for anti-malarials, facilitating affordability of its products in private markets, and helping its partners with ensuring acceptability by global and national agencies.

It is vital for MMV to have an in-depth understanding of the issues of pricing, supply and affordability to make sure first of all, that these activities make strategic sense and secondly that it has the competency to pursue them. In the following section we discuss the issue of pricing and affordability of MMV's products. We look at the manufacturer's pricing decision to examine what impact this has on uptake and to analyze the potential value MMV can add to challenges related to uptake in this context.

5. Decision analysis to answer key access related questions

As illustrated in the previous section, existing theoretical frameworks in economics and strategy are not adequate to address the decision problem faced by MMV. Many of the issues require more in-depth operational analysis before MMV can decide whether or not to engage in these activities and what role should it play. In this section we use stylized models with parameters obtained from different public data sources and MMV's field research in Uganda between May and September 2007 to analyze these issues (MMV Uganda Report, 2007). We use our findings to demonstrate the value of carrying out some access related activities to MMV's top management.

When the pharmaceutical partners of MMV launch the new products into markets in malaria endemic countries, the pricing decision is one of the key variables that determine the reach and uptake of these products. We start our analysis by looking at how a manufacturer will price its new products developed in partnership with MMV and demonstrate the need for a mechanism to reduce prices (e.g. a global subsidy). We then delve deeper into price and capacity relationships, the impact of forecasting, and variables that MMV should consider in its contractual terms with its pharmaceutical partners.

5.1 Pharma Pricing of products co-developed with MMV

In order to understand affordability and uptake we need to understand how MMV's pharmaceutical partners would price their products in the absence of any contractual obligations on pricing. Given that it is difficult to assess the marginal cost of production of a new drug, our analysis starts with the assumption that the first new products out of the MMV portfolio are likely to have manufacturing technologies very similar to existing ACTs and will be based on similar raw materials. Novartis sells its ACT Coartem® on a no-profit/ cost-recovery only basis to public sector and NGO buyers (Novartis website). We use the public sector price of Coartem® as a proxy for the marginal cost of some of the early products that will be launched from the MMV portfolio. In typical pharmaceutical price setting problems the monopolistic or quasi monopolistic manufacturer prices above marginal cost to recover its reward for innovation investments. This leads to a wealth transfer from patients to the monopolistic pharmaceutical manufacturer. In the case of products from the MMV portfolio a large part of the drug development costs were financed by MMV, hence the extent of fixed R&D cost recovery by manufacturers from the selling price of these drugs will be minimal. In addition, many manufacturers develop and manufacturer drugs for malaria as a part of corporate social responsibility and not necessarily profit maximization. Given these dynamics, even if the manufacturers price the drugs close to their marginal cost, there will be a large "deadweight loss" from forgone purchases which would have taken place if the price were lower. Large segments of the population which are poor may not purchase a new drug developed by MMV because of its high price, and as a result either do not obtain treatment for malaria or may look for an inferior substitute drug such as CQ or SP. Despite being significantly less effective, these drugs still have a large market share in many

countries due to their price. Being simpler to manufacture, these products are 10-20 times less expensive than the marginal cost of MMV's drugs.

Taking the case of Uganda, we start by understanding the price vs. potential demand curve for anti-malarial drugs. MMV has carried out one pilot, and operational research projects in Uganda. It is currently carrying out another, thus it is a well a suited a case example. We model the way in which the shape of the demand curve changes the profit-maximizing price. In malaria endemic countries the willingness of patients to pay for the drug is poor because they have to pay out of pocket (there is almost no insurance). Public provision of drugs is usually free but availability and access are problems as highlighted previously. We model the uptake of the drug as the percentage of the malaria sufferers in the country who earn a daily wage that is greater than the cost of one full course of treatment. Table 3 and 4 below depict these calculations.

PPP GDP in US$	41,885 ,000
GINI Index	43
Population	32,369,558
Malaria cases per year	12,792,759

Table 3: Demand and Income Parameters Uganda

	Fraction	Share of GDP in %	Share of GDP in'000 $	Population of income quintile	# of malaria cases in income quintile	Daily income in US$
Lowest	10%	2.3	963	3,236,956	1,279,276	0.298
Next	10%	5.9	2,471	3,236,956	1,279,276	0.382
Second	20%	10.0	4,189	6,473,912	2,558,552	0.647
Third	20%	14.0	5,864	6,473,912	2,558,552	0.906
Fourth	20%	20.3	8,503	6,473,912	2,558,552	1.313
Highest	10%	49.7	20,817	3,236,956	1,279,276	3.215
Top	10%	34.9	14,618	3,236,956	1,279,276	4.516

Table 4: Percentage of the malaria sufferers related to levels of income (Source: World Bank development Indicators, World Malaria Report, CIA Factbook, UN Stats)

In table 4 we compute the income distribution and estimate daily incomes in US$ for different socio-economic quintiles in Uganda's population. This allows us to estimate the fraction of the population that can afford a full course treatment at different price points. For example, we see more than 40% of the population would not be able to afford the product even if it was sold at its marginal cost of $0.8 per average[1] treatment course.

Figure 6 depicts the overall demand for anti-malarial drugs in Uganda at different price points using the calculations in table 4. The shape of the curve shows that even within a low price range ($0.5 - $1.0), demand declines steeply as a result of price increases. This rate of decline flattens out however after we reach a price of around $1.3. The shape of this curve has wide ranging implications for how a pharmaceutical manufacturer would choose to set its price in such a market.

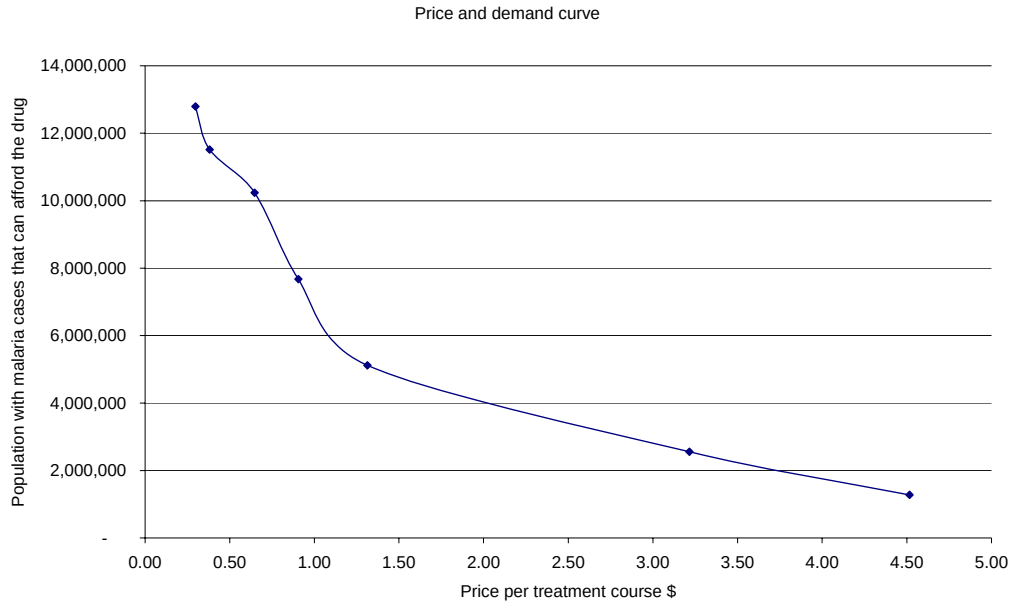

Figure 6: Prices and potential demand curve for Uganda

We acknowledge that figure 6 considers only potential demand, while actual demand is influenced by many other factors and product attributes. This analysis assumes that the willingness-to-pay is the same (1 day of wage) across all income quintiles whereas in reality it varies across population sub-segments based on income. Similarly, we assumed that the incidence of malaria is the same across all income

1 We use average to reflect the fact that the treatment course and its price varies with age and weight of the patient. Adult treatments are more expensive than child treatments.

quintiles which may not always be true. The purpose of this analysis is only to provide guidance and insights into the price setting problem. It is not meant to generate actual demand estimates for Uganda at different price points.

Using the demand curve in figure 6 we compute how a profit maximizing manufacturer will choose to set its price. As the manufacturer increases price, it is able to capture more profits from each sale although the size of the market becomes smaller. The profit maximizing price thus depends on the shape of the demand curve in figure 6. Figure 7 shows the manufacturer's revenue and share of the population covered at that price. As illustrated in figure 7, the revenue maximizing price for a manufacturer is close to $1.9 per treatment course and only 28% of those requiring malaria treatments will be able to afford the anti-malarial at that price. Thus there is a clear conflict between the objective of maximizing revenue and ensuring that a large fraction of the population has access to the product.

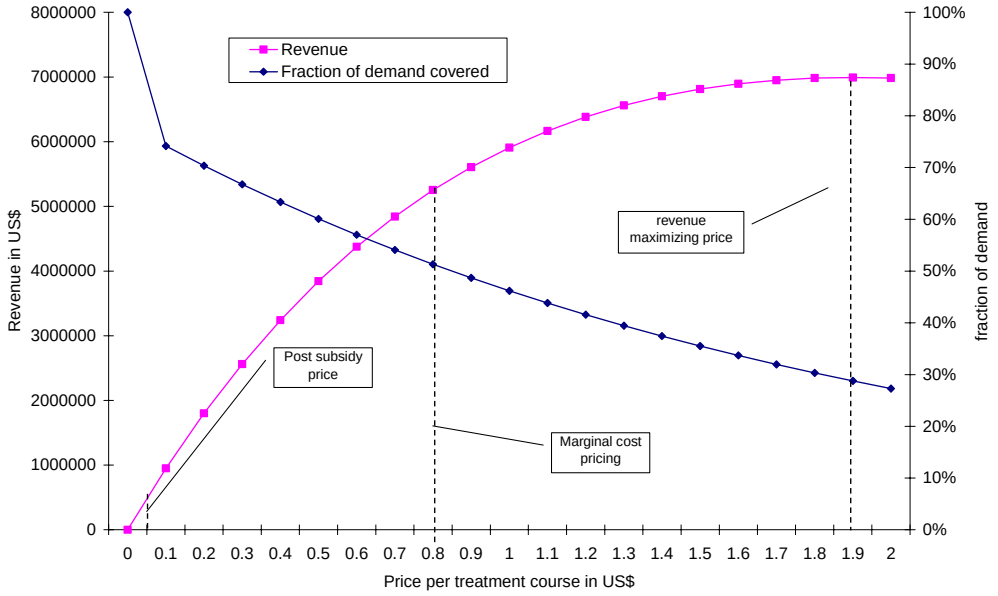

Figure 7: Revenue curve and revenue-maximizing price for a manufacturer for the Uganda anti-malarial market

MMV seeks to ensure public and NGO sector pricing by its partners do not exceed USD 1.00 for a single adult treatment and USD 0.50 for a pediatric treatment. However, limiting the price charged by manufacturers through contractual clauses instead of looking at methods of addressing the affordability gap by other

interventions presents another set of challenges as discussed in section 5.3. The two approaches may be required in complement, rather than as alternatives.

Additionally, contractual price restrictions can only force a manufacturer to price the drug at its marginal cost. Even if the manufacturer chooses a price equal to its marginal cost (marginal costs are computed based on the average adult treatment course of Coartem®) only about 50% of the overall anti-malarial demand can be satisfied at that price. The coverage estimates are in fact optimistic as they are based on the manufacturer's selling price. In reality (as shown in figure 3) the manufacturer's selling price is only a small component of the end retail price. Thus ensuring high affordability is not possible by bringing down manufacturer's prices unless technological innovation drastically reduces the cost of manufacturing.

Another solution could be a differential pricing arrangement where one population sub-segment pays less than the marginal cost and the manufacturer recovers its costs disproportionately from the two segments. Such an arrangement may not be feasible in this case, because of physical and informational arbitrage between the two population segments.

5.2. Subsidizing anti-malarial drugs and MMV's potential role

One possible solution being discussed (Arrow 2004, Laxminarayan 2006) to address the affordability issue is to create a global subsidy for ACTs. At its most basic level, the global subsidy would act as a co-payment mechanism to allow governments and private channel importers to purchase ACTs at a price comparable to what they currently pay for less effective alternatives (SP or CQ). This co-payment would enable both public sector and private sector providers to distribute ACTs to patients at significantly reduced prices even if manufacturer prices remain around $0.80. This would also serve to decouple the market coverage from the marginal cost recovery price charged by a manufacturer. However, several operational questions about the design and functioning of such a subsidy need to be answered. Pushing affordability of anti-malarial drugs through interventions such as the global ACT subsidy is essential to ensure that MMV's drugs achieve their required reach. Although MMV cannot become involved in financing or administering the subsidy, it can play a key role in generating operational evidence about the need for such an intervention and in demonstrating its effectiveness.

5.3. Price and investment in production capacity

Close to the stage of final regulatory approval of the drugs, MMV's pharmaceutical partners have to make investments in capacity to manufacture the approved drugs. The manufacturer's incentives to invest in capacity are dependent upon the price it can charge for the product and the accuracy of the long term demand forecast. In this sub-section we discuss how the manufacturer's incentives for capacity investment change with the price of the drug. In sub-section 5.4 we analyze the impact of better forecasting on pricing and capacity decisions.

A manufacturer facing uncertain product demand which is highly price dependent would make capacity planning and pricing decisions in an integrated manner. We consider a manufacturer with a manufacturing cost of $0.80 per average treatment course and use the demand elasticity calculations for Uganda to estimate the share of total global demand that it can capture at a given price (details of model in Appendix).

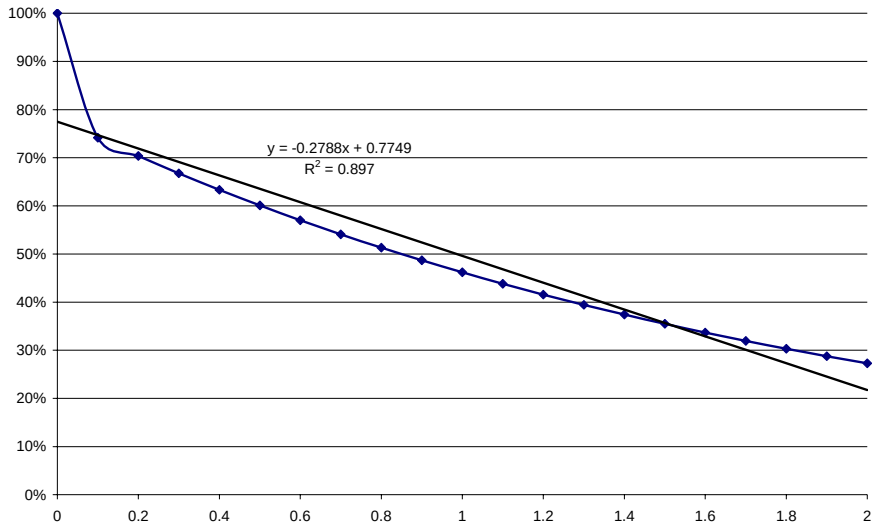

Figure 8: Price and share of demand captured (based on Uganda)

We use the Uganda data as a global proxy to fit the best linear curve to capture the relationship between price and share of demand (Figure 8). From the curve fitting as illustrated in Figure 8, our estimate of the share of global demand captured by a manufacturer at a price *p* is as follows:

$$D = 0.7749-0.2788p$$

Using the estimates of global demand obtained from various independent studies (Roll Back Malaria 2009) we create 3 scenarios: pessimistic, most likely and optimistic demand. Table 5 shows these estimates and also shows the potential demand in each scenario that will be captured by a manufacturer who prices at $1.9 (the revenue maximizing price)

Demand scenario	Global	Potential demand captured at p = $1.9
Pessimistic	80	22
Most Likely	100	27
Optimistic	140	38

Table 5: Demand estimates in Million average treatment courses

Our earlier analysis was based on the assumption of deterministic demand. Using the demand scenarios in table 5 we now model the uncertainty in demand through a triangular distribution. We had seen in the previous section that a profit maximizing manufacturer would choose to price its product around $1.9. In the presence of demand uncertainty and the simultaneous choice of price and capacity, the manufacturer's problem becomes more complex. The manufacturer's decision problem now consists of finding the best price and capacity combination while considering that changing the price decreases the share of the global demand captured by its products. In figure 9 we first look at the problem of finding the optimal capacity investment for a given price. Obviously, the manufacturer makes no capacity investment as long as the price charged is lower than its marginal cost of production. Once the price charged is over its marginal cost of production, it makes a large capacity investment. Mean demand is high and profits are maximized by covering a large fraction of the potential market. However, as the price increases, the size of the market covered decreases, hence the capacity investment decreases as well.

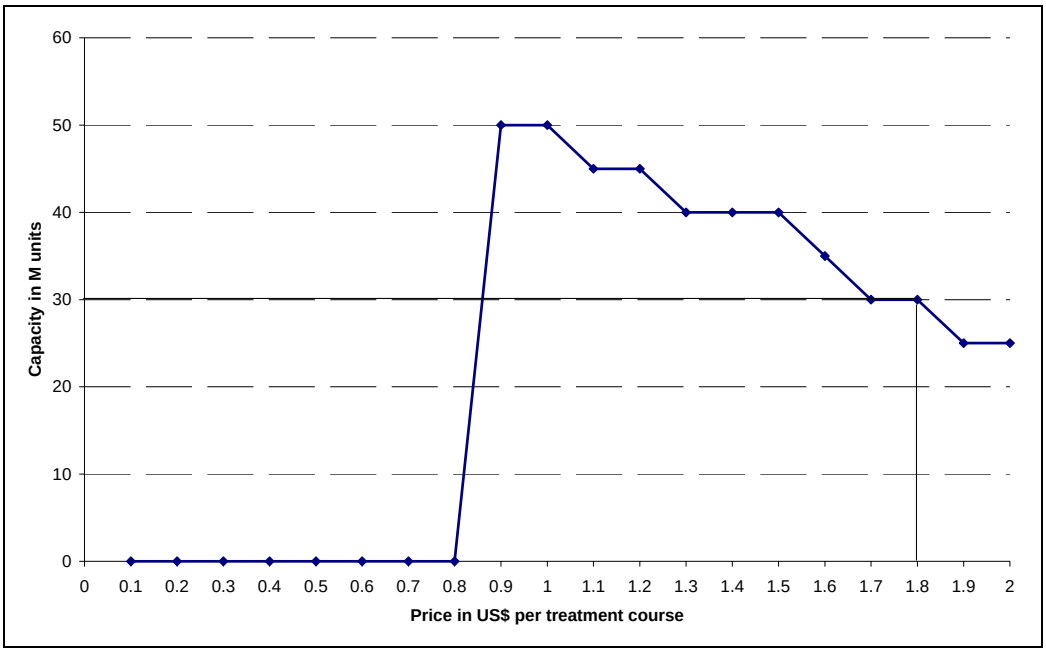

Figure 9: Capacity invested by the manufacturer at different manufacturer selling prices

Interestingly, we found that the manufacturer's incentive to invest in capacity falls as the price it charges increases. As the manufacturer charges a higher price, many effects occur simultaneously. The demand distribution shifts and also the profit margin per unit (and hence the opportunity cost of lost sales) becomes higher. Again, we try to show these effects one by one. As an example, Figure 10 depicts how the distribution of demand changes with an increase in price from $1.0 to $1.8.

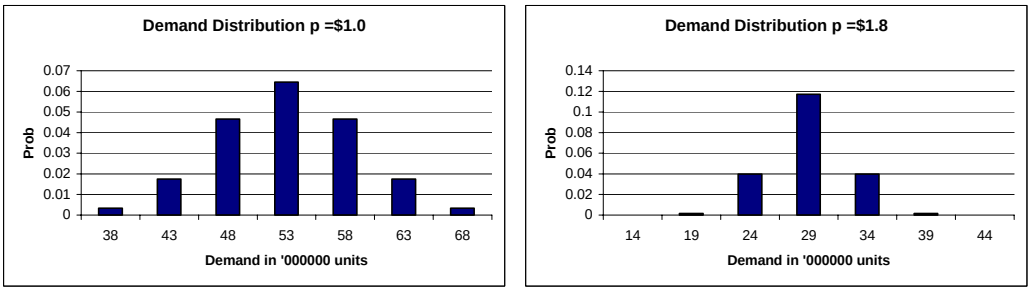

Figure 10: Shift in demand distribution for the manufacturer as price increases

Looking at this effect alone would suggest that price increases lead to decrease in the mean size of the market because of the downward sloping demand curve and this will push the manufacturer's incentive to invest in lower capacity.

However, as price increases, another effect occurs; the per-unit margin of the manufacturer also increases. Not being able to fulfill any demand due to capacity shortfalls now becomes more expensive for the manufacturer which chooses a higher capacity buffer to protect itself against demand uncertainty. The combined net effect depends upon which of the two effects supersede. Figure 11 depicts how capacity investment and profit are altered as a result of price changes from the manufacturer. For the set of cost and demand distribution parameters used we found the following: higher shortage costs resulting from the increased price of the drug leads to higher capacity investment. However, this is not enough to offset the effect of lower mean demand (and hence lower capacity investment) due to increased price. The rate of decrease in capacity installed will be lower than the rate of decrease in the fraction of demand covered.

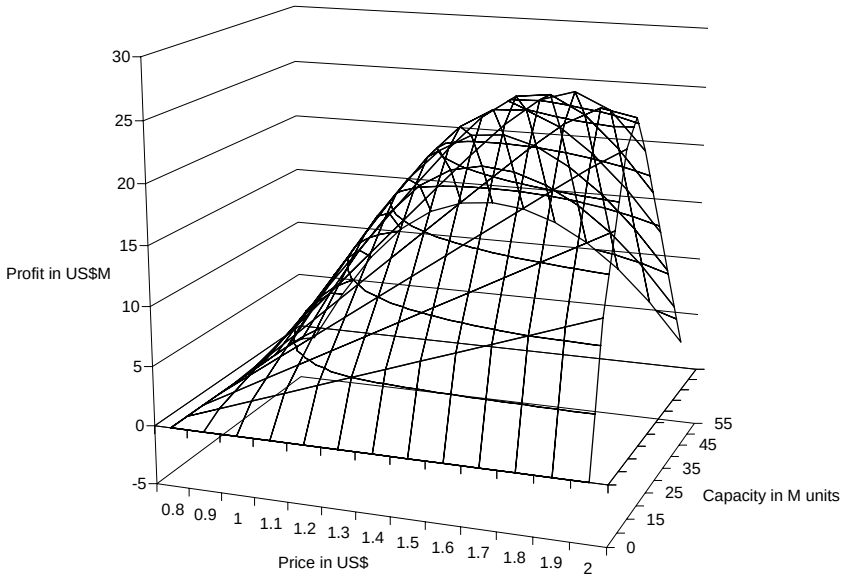

Figure 11: Manufacturer's profit and capacity installed at different manufacturer selling prices

The profit maximizing manufacturer chooses a price of $1.8 and a capacity of 30 million treatments both of which are sub-optimal from a social planner's perspective (see figure 11 and also note that at this price the product remains unaffordable to most parts of the population except the highest socio-economic quintiles). Recall that the manufacturer's profit maximizing price in the absence of demand uncertainty and capacity investment was $1.9. Thus we see that explicitly

accounting for demand uncertainty leads to the manufacturer choosing a slightly lower price than under the assumption of demand certainty.

This analysis also reveals that for the set of parameters relevant to this problem, restricting the manufacturer's price to lower its profit maximizing price leads to larger investments in capacity owing to the market expansion effect. If MMV wants to ensure enough supply of its products, it has to be intensely involved in ensuring that its pharmaceutical partners set reasonable prices. It will also benefit from other interventions such as the global ACT subsidy which can ensure that high price and poor market capture do not lead to socially sub-optimal investments in capacity.

5.4. Demand forecasting and its impact on price and capacity

We saw in the previous section that demand uncertainty has a significant effect on capacity planning and price setting. Accurate demand forecasting for global health products has been noted to enhance available capacity and supply (Levine et al 2008). We conducted what-if analysis on the stylized model and framework in the preceding sections, to analyze the effect of more accurate demand forecasts on the price and capacity decision of the manufacturer. To model the effect of better forecasting we chose a mean preserving distribution shift (see table 6). This is one specific example of using the model to understand the inter-play of various effects on price, capacity and market reach. We find that MMV could potentially play a role in helping to generate better demand forecasts for its products and the anti-malarial market as a whole.

Global Demand estimates	Original	Through Better Forecasting
Pessimistic	80	95
Mean	100	100
Optimistic	140	125
Mean	106.67	106.67
Std. Deviation	12.47	6.56

Table 6: Mean preserving distribution shift modeling the effect of better forecasting

The effect of increased forecast precision on capacity investments is not intuitive in an environment where the manufacturer sets the price and capacity at the same time. What we observe here (figure 12), is that as forecasts of potential market size become more precise, the manufacturer invests in more capacity even at lower prices (even though the profit maximizing price and capacity remain the same).

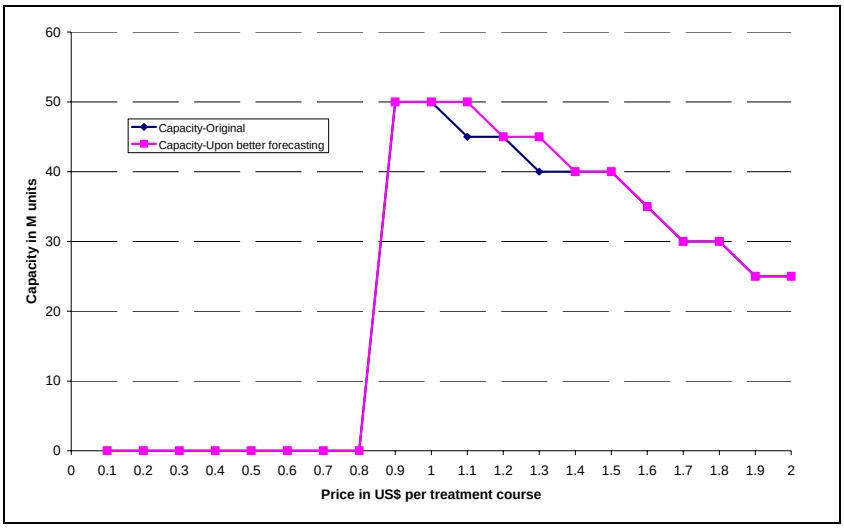

Figure 12: Change in capacity installed due to higher forecast precision

This section has examined the impact of pricing on demand and by extension on the manufacturer's capacity investment. It demonstrates that the investment of MMV in improving estimates of potential demand or anti-malarial market-size will lead to manufacturers investing in higher capacity. The model suggests that if MMV were to include selling price restrictions in its contracts with its pharmaceutical partners, or its pharmaceutical partners' price at marginal cost instead of revenue maximizing price, investments in improving estimates of potential demand/ anti-malarial market-size will result in higher installed capacity for MMV's products.

6. Conclusions

The markets for anti-malarial treatment in the developing world do not function well. When faced with the question of how to approach the access and delivery aspect of their mission, MMV needed to identify what areas in access they should get involved in. Existing theoretical frameworks are not sufficient to answer all of the questions surrounding the issue of access and delivery of anti-malarial treatment. They stop short of examining the operational aspects, such as the misalignment of incentives regarding pricing, demand forecasting, manufacturing and production, procurement, distribution and delivery. Each of these is a determining factor in the uptake of drugs. Our approach is important to public-private development organizations like MMV, particularly if they are moving from an original goal of development into that of access. This paper offers MMV and their stakeholders a systematic framework and approach of analysis. The trade-off curves

we develop are very useful to help MMV focus on the right tasks and allocate resources to the right efforts to maximize its impact on uptake. Our research provides MMV with the tools to develop a clear strategy to approach their role in access and delivery of anti-malarial drugs to patients in endemic countries.

This paper identifies the main challenges in ensuring the uptake of anti-malarial drugs as a result of factors related to acceptance, affordability and availability. It then examines MMV's role as a public private partnership in tackling these issues. We look at transaction-cost theory, core-competency theory, global public good creation, and MMV partner needs to select what activities within access MMV should get involved in. We find that MMV should initially focus its access activities on market sizing and demand forecasting, developing better understanding of the distribution system for anti-malarial treatments, facilitating affordability of its products in private markets, and helping its partners with ensuring acceptability by global and national agencies.

Stylized models are used to understand the need and potential benefits from MMV's involvement in these areas. We focus in particular on the issues of pricing and affordability, and their impact on the uptake of MMV's products. Our analysis shows that a manufacturer's choice of price, even when set at the level of marginal cost, does not lead to high market coverage. It is therefore in MMV's interest to support external interventions such as the global subsidy. It should do that by generating operational evidence which can help answer some of the design questions of the subsidy.

An examination of the impact of revenue maximizing price levels on manufacturers' capacity investment shows that prices set at the level of revenue maximization may lead to lower capacity investment. This occurs as a result of a decrease in market size. MMV can play an important role in tackling this problem. Investments by MMV in improving estimates of anti-malarial market size or demand forecasts will ensure there is sufficient supply capacity for its products. In the absence of such efforts, manufacturers' capacity investment could be lower than what is required to meet MMV's objective of large market coverage.

Based on our analysis, MMV's consultations and deliberations with its other donors and key partners, MMV has created its strategic framework in the area of access as depicted in Figure 10 below. This framework defines MMV's access role to

include the activities that were demonstrated as key using the analysis presented in table 2 and its detailed operational reasons in subsequent sections.

	Objectives			
		Support adoption	**Expand product reach**	**Shape product development**
Activities	**Collect and analyze information**	- Regulatory and policy processes - Barriers to rapid uptake	- Market research - Supply and pricing surveys in informal sector	- Market data to inform target product profiles and packaging
			- Demand forecasting	- Assess impact of OTC rescheduling
	Build awareness and advocate	Country work - Road shows - Information meetings - Advocate for policy change	- Advocate for improved market information and sustainable financing - Disseminate information (website, conferences	- Advocate for norms and branding to protect ACT
	Support MMV products	- Support inclusion of registered products into guidelines / prequalification - Work with country decision maker, WHO, and funders	- Product access/launch plans for target segments	- Participate in product teams - Support label extension studies
			- Supply chain support	- Conduct Phase IV and pharmacovigilance studies - Monitor drug resistance

= MMV role is supportive and relies on working together with external partners

Figure 13: MMV's access strategy framework (Source: MMV)

Using the findings from this research, MMV is now moving ahead with several activities and operational pilots in the areas of subsidizing anti-malarial drugs for poor populations, estimation of demand and market sizing. It has launched a pilot to distribute subsidized ACTs via the private sector channel in six districts of Uganda which will inform operational issues in the design of the global ACT subsidy.

MMV has built on the standard methodology of the WHO and Health Action International to assess prices, availability and supply chains and effectively used this in its market mapping work in Uganda. It is also delving deeper into analyzing and understanding the market for its drugs by leveraging the work of other partners such as ACTWatch (www.ACTwatch.info) which is a five-year study to assess the price, availability and structure of the anti-malarial market in six countries in Africa.

By carefully strategizing and selecting the activities they should get involved in, MMV's access and delivery group has been able to focus its strengths and is now well poised to undertake the challenges in ensuring access to anti-malarials in the poorest regions of the world.

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Appendix

A simple model for simultaneous capacity and price decision by manufacturer facing uncertain demand

Consider a price setting pharmaceutical manufacturer that produces a single product for malaria, faces a random price dependent demand function, and has to jointly determine the capacity to create for the product *Q* and the selling price *p*. The manufacturer's marginal cost of production is *c*. If demand exceeds capacity there is no additional loss of goodwill except the lost margin and excess capacity cannot be sold or salvaged. Fixed investments in R&D are not recovered through price but financed through other mechanisms such as MMV.

The global demand for anti-malarials is given in the table A1 below (RBM 2009)

Demand scenario	Global
Pessimistic	80
Most Likely	100
Optimistic	140

Table A1: demand scenarios for global ACT demand

This is however the total market for anti-malarials; the fraction captured by the manufacturer at any given price p is given by 0.7749-0.2788*p*

For example a manufacturer selling at p = $1.9 will only capture 24.5% of this potential demand. We assume the effect of price applies equally to each demand scenario. Thus the demand captured at p=$1.9 for each scenario will be as tabulated in A2 below

Demand scenario	Potential demand captured at p = $1.9
Pessimistic	22
Most Likely	27
Optimistic	38

Table A2: Potential demand at *p* =$1.9 for different global ACT demand scenarios

Let $\tilde{D}$ denote the random demand. Let *F*(.) denote the CDF of the demand distribution and let *f*(.) be its corresponding PDF.

We approximate the random demand $\tilde{D}$ using a normal distribution with parameters selected based on the above data assuming the three scenarios (pessimistic, most likely and optimistic) are a triangular distribution. The parameters of the normal distribution fitted to the scenarios in the table above are

Mean	26.152
Std. Deviation	3.0579

Thus for each price *p* the resulting distribution of demand *D* can be estimated as a normal distribution $\sim N\left(\mu(p),\sigma(p)\right)$

For instance at price *p* = $1.0 the resulting distribution for demand will have a mean of 52.917 and standard deviation of 6.187

The manufacturer's profit is given by

$$\Pi^m = \begin{cases} (p-c)Q & if\ \ Q \le D(p) \\ (p-c)D(p) & if\ \ Q > D(p) \end{cases}$$

Where $D(p)$ represents the realized demand at price *p*

And the expected profit can be written as

$$E\left[\Pi^m\right] = (p-c)Q\int_{D=Q}^{\infty} f(D)dD + (p-c)\int_{D=0}^{Q} Df(D)dD$$

The manufacturer then solves the following two variables maximization problem

$$Max_{p,Q} \quad E\left[\Pi^m\right] = (p-c)Q\int_{D=Q}^{\infty} f(D)dD + (p-c)\int_{D=0}^{Q} Df(D)dD$$

Characterizing the optimal solution to this problem requires choosing a form of $D(p)$. We have used a multiplicative relationship we have used between price and potential demand captured for each of the demand scenarios and we fit a normal distribution to the resulting demand scenarios for a given price. Thus, instead of characterizing the optimal *p* and *Q* analytically we solve this two variable problem by exhaustive search over a set of capacity and price options and comparing the total profits of the manufacturer for each case. As shown in table A2 below by ssing the two-way table option in Excel we determine the optimal values of *p* and *Q*.

	capacity →										
price	0	10	15	20	25	30	35	40	45	50	55
↓ 0.1											
0.8											
0.9	0.00	1.00	1.50	2.00	2.50	3.00	3.50	3.99	4.38	4.41	3.53
1	0.00	2.00	3.00	4.00	5.00	6.00	7.00	7.96	8.71	8.72	7.35
1.1	0.00	3.00	4.50	6.00	7.50	9.00	10.49	11.88	12.79	12.41	10.25
1.2	0.00	4.00	6.00	8.00	10.00	12.00	13.97	15.68	16.39	15.16	12.15
1.3	0.00	5.00	7.50	10.00	12.50	14.99	17.39	19.16	19.13	16.79	13.16
1.4	0.00	6.00	9.00	12.00	15.00	17.98	20.66	21.98	20.66	17.35	13.43
1.5	0.00	7.00	10.50	14.00	17.50	20.91	23.52	23.62	20.90	17.06	13.07
1.6	0.00	8.00	12.00	16.00	19.98	23.66	25.44	23.75	20.10	16.12	12.12
1.7	0.00	9.00	13.50	18.00	22.43	25.85	25.77	22.53	18.57	14.57	10.57
1.8	0.00	10.00	15.00	19.99	24.66	**26.69**	24.32	20.43	16.43	12.43	8.43
1.9	0.00	11.00	16.50	21.95	26.11	25.40	21.69	17.69	13.69	9.69	5.69
2	0.00	12.00	18.00	23.68	25.55	22.35	18.36	14.36	10.36	6.36	2.36

Table A3: Manufacturer's Profit as a function of price and capacity

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