Global Health Forecasting Working Group
Background Paper

# Mapping and Realigning Incentives in the Global Health Supply Chain

By Prashant Yadav, Kirsten Curtis and Neelam Sekhri

**Abstract**

Poor allocation of risks among the constituents of a supply chain results in a misalignment of incentives, leading to over-reactions, unnecessary interventions, second guessing, mistrust, and distorted information – ultimately degrading its ability to match supply and demand. This study assesses the current allocation of operational risks and their impact on the incentives of different players in the global health supply chain, focusing on the case of fixed-dose artemisinin-based combination therapy for malaria as an illustrative example.

Currently, there is a highly non-optimal allocation of risks in this supply chain, where constituents that have the best knowledge about demand uncertainty, or the highest ability to resolve part of this uncertainty, or have the highest potential to benefit from this uncertainty reduction, do not necessarily carry its corresponding risks. This and other improper risk allocations lead to misaligned incentives for accurate forecasting, sharing demand/supply information in this supply chain. Similarly, an asymmetric risk structure for the quality regulators does not provide them the right incentive to quickly approve more drugs by higher resource commitment.

The authors recommend establishing a global health infomediary to overcome the uncertainty due to the opacity of data from the various supply chain nodes. Funding agencies should also adopt a risk-sharing approach based on rolling partially-flexible purchase commitments, which would lead to an economically optimal sharing of risks and would eliminate some of the incentive misalignments, as well as a broader use of framework contracts. Finally, manufacturers should explore the potential for a joint demand driven supply-hub to respond more rapidly to order and reduce the overall reliance on demand forecasts.

This paper informed the deliberations of the Center for Global Development's Global Health Forecasting Working Group and is cited extensively in their final report, *A Risky Business: Saving Money and Improving Global Health through Better Demand Forecasts.*



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# Mapping and Realigning Incentives in the Global Health Supply Chain

## Based on the Supply Chain for Artemisinin Combination Therapy Treatments for Malaria

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# Executive Summary

Poor allocation of risks among the constituents of a supply chain results in a misalignment of incentives. Misaligned incentives create effects such as over-reactions, unnecessary interventions, second guessing, mistrust, and distorted information; all of which can eventually lead the supply chain into a “risk spiral” and severely degrade its ability to match supply and demand. The complex nature of economic and information flows in global health supply chains make these incentive misalignments difficult to detect. This study views global health supply chains from the lenses of supply chain scientists to assess the current allocation of operational risks and their impact on the incentives of different players. We use the supply chain for artemisinin based combination therapy (ACT) as an example to illustrate our approach.

We find that currently there is a highly non-optimal allocation of risks in this supply chain. Constituents that have the best knowledge about demand uncertainty, or the highest ability to resolve part of this uncertainty, or have the highest potential to benefit from this uncertainty reduction, do not necessarily carry its corresponding risks. This and other improper risk allocations lead to misaligned incentives for accurate forecasting, sharing demand/supply information in this supply chain. Similarly, an asymmetric risk structure for the quality regulators does not provide them the right incentive to quickly approve more drugs by higher resource commitment.

To overcome the uncertainty due to the opacity of data from the supply chain nodes (manufacturer, funding agency, recipient country, procurement agent), we recommend the establishment of a global health infomediary. This remedies the inherent incentive problems that may be preventing accurate forecast development and information sharing in global health supply chains.

We then recommend a risk-sharing approach based on rolling partially-flexible purchase commitments from the funding agencies to the manufacturers. This leads to an economically optimal sharing of risks and would eliminate some of the incentive misalignments. We recommend the funding agencies to engage in “framework contracts” with manufacturers and compare this approach to pooled purchasing based on our characterization of the sources of efficiency in procurement.

We describe the concept of a supply-hub with co-located inventory from different manufacturers to decrease the time of delivery after order placement. This enables the manufacturers to better manage their short-term risk and creates better preparedness for short-term demand spikes and their associated shortage risks.

We also briefly discuss the implications of the ACT global subsidy and similar interventions in the private sector market.

# Abbreviations

| | |
|---|---|
| ACT | Artemisinin Combination Therapy |
| AL | Artemether-Lumefantrine Combination therapy |
| AQ | Amodiaquine |
| ARV | Anti Retro Viral (for HIV/AIDS) |
| CDA | Chlorproguanil -Dapsone-Artesunate |
| CGD | Center for Global Development |
| CHAI | Clinton HIV AIDS Initiative |
| CQ | Chloroquine |
| EML | Essential Medicines List |
| FDC | Fixed Dose Combination |
| GFATM | Global Fund to fight AIDS, TB and Malaria |
| GMP | Global Malaria Program |
| GMP | Good Manufacturing Practices |
| HIV | Human Immunodeficiency Virus |
| IAPSO | UNDP's Inter-Agency Procurement Services Office |
| ICH | International Conference on Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use) |
| IDA | International Drug Association |
| IDPF | International Drug Purchasing Facility |
| IFPMA | International Federation of Pharmaceutical Manufacturers & Associations |
| JSI | John Snow International |
| ITNs | Insecticide Treated Nets |
| L | Lumefantrine |
| M2S2 | Malaria Medicines and Supply Services |
| MMSS | Malaria Medicines and Supplies Service |
| MMV | Medicines for Malaria Venture |
| MoU | Memorandum of Understanding |
| MQ | Mefloquine |
| MSF | Médecins Sans Frontières |
| MSH | Management Sciences for Health |
| PEPFAR | Presidents' Emergency Plan for AIDS Relief |
| PIC/S | The Pharmaceutical Inspection Cooperation Scheme |
| PMI | President's Malaria Initiative (US) |
| PSM | Procurement and Supply Management |
| RBM | Roll Back Malaria Partnership |
| UNDP | United Nations Development Program |
| UNICEF | United Nations Children's Fund |
| USAID | United States Agency for International Development |
| WHO | World Health Organization |

# 1 | Introduction

Several forces are converging to encourage the global health community to focus on creating supply chains for global health products in which the objectives of all the constituents are more tightly aligned. Firstly, there are substantial amounts of money coming in from various streams for global health programs but most programs are distraught with the perils of poor matching of demand and supply, the core role of chain management. Secondly, there is an emerging consensus that while there is need for accurate demand forecasting for global health products, some unavoidable uncertainties in the forecast will continue to exist. Hence, supply chain management strategies used in other industries with high forecast uncertainties should be given due consideration. Thirdly, the initial results of supply chain management based interventions in certain specific sectors such children's vaccines have been extremely encouraging.

In the manufacturing and distribution of global health products, the vagaries of the demand market and the long production and ordering cycles do not allow the perfect matching of supply and demand. There always exists a risk of either having too much or too little in the supply chain. It is not pragmatic to assume that this risk can be entirely eliminated by means of better forecasting or demand management. The key question then becomes how should the unavoidable risk in a supply chain be allocated amongst it constituents and how does the allocation impact the end-objective of the supply chain; in this case the enhanced and timely availability of essential drugs to the developing world. Poor risk allocation results in a misalignment of incentives for the supply chain constituents, and the complex nature of economic and information flows in these supply chains makes the incentive misalignments difficult to detect. The poor allocation of risk in an already complex supply chain also increases "chaos" within the supply chain. These chaos effects result from over-reactions, unnecessary interventions, second guessing, mistrust, and distorted information, all of which can eventually lead a supply chain into a "risk spiral" (Christopher and Lee 2005).

Therefore, any initiative focused on improving the performance of this supply chain needs to start with an assessment of the current allocation of risk and its impact on the stakeholders' incentives for activities that are key for the efficient operation of a supply chain.

The objective of this study is to view the global health supply chain from the lenses of supply chain scientists. This report attempts to accomplish two main tasks: 1) to assess the current allocation of risks in the current supply chain for global health products and its impact on the incentives of different players; and 2) to consider a few specific interventions that would allow to remedy these incentive misalignments either through better risk-sharing or, if possible, risk- mitigation. To narrow the focus, we analyzed the supply chain for pharmaceutical products recommended for the treatment of malaria. There is overall consensus that there is some "low hanging fruit" in the area of malaria (More than 1.2 million people die each year from malaria, most of whom could be potentially saved with little aid money) and the

complexities in this supply chain are more tractable so that it can be used to demonstrate the quick improvements that can result from such interventions.

# 2 | Malaria and ACTs

According to recent estimates, between 300 million to 660 million cases of malaria occur every year (WHO 2005, Snow et al 2005). More than 1.2 million mortalities a year are attributed to malaria, roughly 75% of which are among children below six-years of age (WHO 2005).The estimated health and economic toll due to malaria is tremendous. Every year, Africa alone loses US$12 billion due to malaria in direct and indirect costs.

For the last half-century or more, malaria has been treated with drugs such as quinine, chloroquine (CQ), amodiaquine (AQ), mefloquine (MQ), and lumefantrine (L). However, in the last two decades a high degree of resistance has started emerging in the malaria parasite against these drugs, predominantly against chloroquine (CQ). This has resulted in increased malarial deaths in Africa, even though the patients were getting the (ineffective) CQ treatment. The biomedical community agrees that the evolution of drug resistance is an inevitable consequence of genetics and natural selection and any single drug used to treat malaria over an extended period of use will lead to the development of resistance. However, the development of resistance can be stopped or prolonged if two (or more) effective anti-malarial drugs with different mechanisms of action are simultaneously used.

Drugs in which one of the anti-malarials is an artemisinin compound have been found to be particularly effective in the treatment of malaria and have the lowest chances of the malarial parasite developing resistance against it. In the recent years, the WHO has recommended a combination of at least two anti-malarial drugs, one of which is an artemisinin derivative for treating malaria. This treatment option is called Artemisinin Combination Therapy (ACT) and is currently the recommended first-line treatment option for malaria, according to WHO. The use of single-drug therapies that are either artemisinin based or non-artemisinin based, however, continues unabated in many regions of Africa and Asia, especially in the private sector. Many new manufacturers of malaria drugs are based in the developing countries and do not have the resources required to obtain approval from an ICH or PIC/S regulatory authority. The WHO has a mechanism to pre-qualify manufacturers to ensure the safety and quality of malarial (and other) drugs that can be procured by developing countries using grants from global health institutions. Currently, the only ACT drug pre-qualified by WHO is Novartis' fixed-dose artemether-lumefantrine combination (AL) sold under the brand name Coartem® in the developing world and as Riamet® in the EU and Australia. The other pre-qualified artemisinin based drug is Arsumax from Sanofi-Aventis, which by itself is a monotherapy, but its co-blistered combination with amodiaquine (AS/AQ) is extensively used as an ACT by many recipient countries. Co-blistered ACTs are not Fixed Dose Combinations (FDC), and therefore are not as effective because of poor usage compliance. A complete list of pre-qualified drugs for malaria is provided in Table 1.

The crux of the problem is that the costs of the ACTs are an order of magnitude higher than the cost of traditional malaria treatment. CQ costs approximately $0.10 per average dose as compared to the $1

price of Coartem[1]. Even when CQ was effective and there were no resistance issues, it did not reach everyone in Africa. With a twenty times higher cost of the ACTs, the endemic countries are unable to cover these costs through the small budgets of their malaria programs. Funding agencies such as the Global Fund to Fight AIDS, TB and Malaria (GFATM), the World Bank, the USAID and various others have come to the rescue of the endemic countries by awarding them grants to procure ACTs. Manufacturers such as Novartis and Sanofi-Aventis have done their share by agreeing to sell anti-malarial products to the public-sector at very affordable prices.

**Table 1. WHO pre-qualified drugs for malaria as of March 29, 2006**

| Brand-name® | Compound | Manufacturer | Remarks |
|---|---|---|---|
| Arsumax | Artesunate | Sanofi-Aventis | Mono therapy |
| **Coartem** | **Artemether/Lumefantrine** | **Novartis** | **Approved ACT** |
| - | Artesunate | Guilin Pharma | Mono therapy |
| Artemotil | Beta-Artether | ARTECEF | Injectible |

### 2.1 Production and Costs of ACTs

Typically, the pharmaceutical industry recovers the R&D costs of new drugs with a high markup over the costs of producing the drug while the drug is still under patent protection. For drugs that have an evenly distributed demand worldwide, pharmaceutical companies engage in differential pricing where the fixed R&D costs are recovered from high markup sales in the developed countries, and prices are kept substantially lower in the developing countries. Unlike the market for Anti Retro-Virals (ARVs) for HIV/AIDS, the market for malaria drugs is almost negligible outside of endemic nations. Thus, this differential pricing mechanism of recovering R&D expenditures clearly fails in this case, and prices can be lowered through either the use of good quality generic manufacturers or convincing original manufacturers to use a R&D+fixed cost amortization model that hinges on very high volumes with very low markups. In this report we assume that either forced by price competition (the presence of an evident threat of qualified generic manufacturers) or due to a sense of corporate social responsibility, the manufacturers will continue to sell these drugs at low(or zero) markups to the developing countries. We thus need to focus on reducing costs to the manufacturers, which would then hopefully get passed on as lowered prices to the endemic countries.

To better understand why the costs of the ACTs are high, we need to look at the current production process and time-lines involved in the manufacturing of ACTs. As depicted in Figure 1 below, the process involves growing the herb-plant, *Artemisia Annua*, followed by the extraction and production of the required artemisinin compound (artesunate, artemether, etc.). The artemisinin compound is then co-formulated with the companion drug substance. The price of the ACTs is therefore driven by both the cost

[1] Public sector prices effective September 2006

of the artemisinin compound and the companion drug substance. For example, in the case of Coartem, the companion drug substance lumefantrine is more expensive as compared to the artemisinin compound or the other possible companion drugs. One ACT adult treatment course contains 0.48 g artemether in the case of AL treatments and 0.6 g artesunate in the case of AS based combinations.

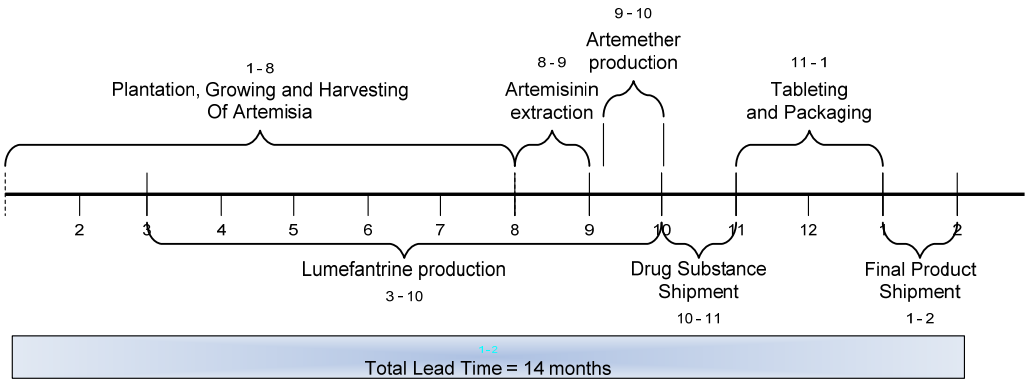



**Figure 1: Time lines in the ACT production process (for Artemether Lumefantrine combination). Based on Coartem data from Novartis**

The total lead-time for the manufacture of AL based ACTs is currently approximately 14 months. This long lead time makes accurate and un-biased forecasts of demand extremely critical for the successful operation of this supply chain. Also noteworthy is that ACTs currently have a short shelf-life of approximately 2 years and the shelf-life of artemisinin is around 18 months. Initiatives focused on reducing the lead-time of the production process using synthetic artemisinin-like products are under consideration and likely to yield a commercialized product around 2008 (MMV).

We argue that a higher demand for ACTs will induce competition among the manufacturers, increase the size of the supply market and can lead to lower prices. However, a higher demand for ACTs cannot be stimulated unless: 1) the malaria affected countries are offered grants and other incentives from the global health financing institutions to adopt ACTs as first-line treatment for malaria and 2) accurate long-term forecasts on ACT demand are made available to existing and potential manufacturers. These forecasts should be presented as scenarios with different assumptions about ACT prices and the level of international funding for malaria. In the next subsection, we look at the historical forecasts, demand, price and supply situation of ACTs.

### 2.2 ACT demand, supply and prices

The demand and supply for ACTs have risen very sharply since 2001 when the WHO recommended the use of artemisinin based products as first line treatment for malaria. The real scale-up in the demand and supply of ACTs occurred starting in 2004 when funding agencies such as the GFATM promoted new

grants and reprogrammed existing ones for ACT procurement instead of the conventional treatment options for malaria. The volumes of ACTs sold annually have reached from a few thousands in 2001 to over 60M in 2006. In the early years of this ramp-up in 2004, the supply chain for ACTs had experienced a severe shortage of artemisinin and lumefantrine resulting in high market prices for the two compounds. This problem has, however, been resolved with more planted acreage to grow Artemisia and more extraction capacity. Novartis, the manufacturer of the only WHO pre-qualified ACT, has also substantially ramped up the production capacity at its two facilities in Suffern, NY and in Beijing, China.

Under a special Memorandum of Understanding (MoU) with the WHO, Novartis has been supplying Coartem on a cost only basis at an average price of $1.57 per treatment for public sector procurement in developing countries. The price of private sector Coartem continues to be in the range of $7-1$10. Effective September 2006, Novartis has further reduced the public sector price of Coartem to an average of $1 per treatment. The prices of other ACTs and mono-therapies from many of the non-qualified manufacturers continue to be lower. Table 2 provides estimated prices for major manufacturers that are currently supplying Coartem. It has been noted that the prices of ACTs, especially those supplied from the generic manufacturers, depends upon the current market price of the API and the quantity ordered (CHAI Study 2006).

**Table 2. Prices of ACTs (adult treatment)**

Source: CHAI Estimates

| Product | Ex-factory price for adult dosage | Supplier |
|---|---|---|
| Coartem | $1.80 | Novartis |
| Generic AL | $1.70 | Cipla |
| AS/AQ | $1.60 | Sanofi-Aventis |
| AS/AQ | $1.20-$1.50 | Cipla |
| AS/AQ | $2.20-$2.30 | Ajanta Pharma |
| AS/AQ | $1.50 | Strides |
| AS/MQ | $2.50-$3.00 | Mepha |
| DHA+ Piperaquine | $1.20 | Holley Pharma |

The demand forecasts for Coartem have been provided on a rolling basis to Novartis from the MMSS group at RBM. Table 3 below details the actual demand, forecasts and installed capacity for Coartem.

**Table 3. Forecasts, Sales and Capacity for Coartem**

Source : Novartis, MMSS

| *All figures in million treatments* | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|
| Forecast Provided in | | | | |
| Dec-04 | 55 | 106 | 109 | |
| Dec-05 | | 64 | 72 | 80 |
| Sep-06 | | 62 [1] | 64 | 80 |
| Actual Sales | 14 [2] | 55 [3] | | |
| Installed Capacity | 33 | 120 | 120 | |

[1] 61.5m =44m treatments actual sales till August 2006 + 17.5m forecasted for Q4 2006

[2] 9m sold till Dec 2005 + 5m in early Jan 2006 that are counted as 2005 sales

[3] 44m sold till August 2006 + 11m expected orders. The manufacturer will carry an additional stock of 5m bringing the total production in 2006 to 59m

Table 3 depicts that the deviations in the long term forecasts for Coartem demand have been extremely high in the early phase. Also, the forecast had to be updated very frequently and large deviations have continued to exist in the forecast updates as well. The manufacturer scaled-up its production capacity to the current level of 120 million treatments based on the initial forecast in 2004-05. However, the realized sales continue to be in the range of 60 million treatments. On the one side, we could argue that there are always learning effects in forecasting and that forecast accuracy will improve based on learnings from the historical inaccuracies. On the other hand, (as will become evident in the following sections of this report), the landscape of this supply chain is likely to become much more complex in the near future. With the additional choices would come additional sources of uncertainty in demand and supply, making forecasting even more challenging. This raises two important questions: 1) Would the current mechanisms of forecasting suffice in the future scenario, or is a radically different approach to forecasting required; and 2) What factors lead to the poor uptake of ACT demand (assuming the initial forecasts were based on a needs-based forecasting model and not a constraint-based demand forecasting model)? While a discussion of what are the technically appropriate methodologies for global health forecasting is beyond the scope of this report (please refer to another report titled “Global Health Forecasting Principles”), we attempt to address both of these questions to some extent.

# 3 | Overview of ACT Supply Chain

The various agencies involved in the manufacturing, financing, purchasing and distribution of ACTs have often cited poor forecasting, inadequate product supply or insufficiency of funds as the reason for poor access to ACTs. In reality, it is the complexity in the processes and interrelationships between these agencies that often obscures the true uncertainties in the demand and supply situation. Sometimes the roles in this supply chain are overlapping and not well understood by many agencies trying to help improve the access of malaria drugs. Therefore, we first try to present a macro-level view of the different stake-holders, their roles and interdependencies in the ACT supply chain. Apart from its use in this specific study, this understanding of the supply chain structure should also assist other global health initiatives related to malaria in making rational policy decisions.

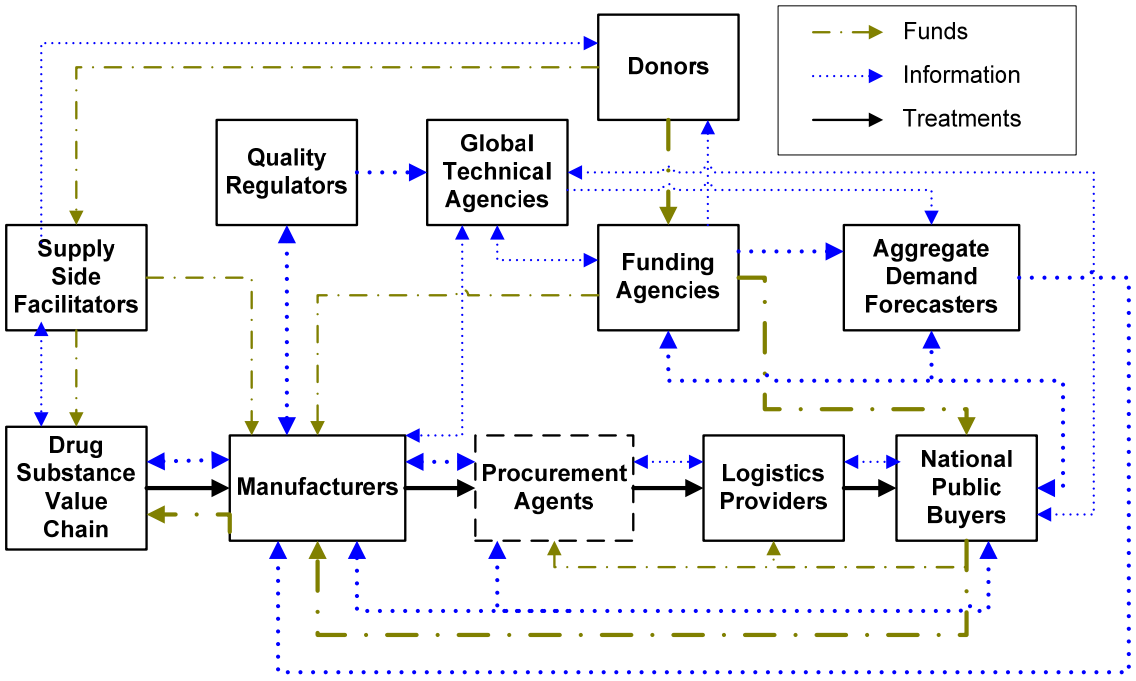



**Figure 2: Stake holders and flows in the ACT supply chain (public sector)**

For definitions and examples of each of these stake-holders refer to the following side-box.

While other flows are not discussed in detail, we choose to describe the process followed by the funding agencies to disburse funds to the recipient countries. Here two very different mechanisms continue to exist. The GFATM, currently the largest funding agency, has a financing model that focuses on country ownership. Although the GFATM is ultimately responsible for the successful use of granted funds, it chooses to pass this responsibility on to the country. Due to this structure, once grants are disbursed, money travels from the funding agency to the buying country. The decisions such as which drug to

purchase and from whom, whether or not to use a procurement agent etc. are delegated to the recipient country. Local Field Agents (LFA) carry out a due diligence on behalf of the GFATM to inspect the distribution infrastructure and confirm that it will have the capacity to support the procurement plan of the buying country. Once this due diligence is conducted, the bid and tendering process starts, and eventually the portion of the grant money earmarked for drug procurement is transferred from the buying country to the manufacturer. There are costs associated with these numerous transactions, including exchange rate risks and conversion fees. In addition, this process takes time, which is an indirect cost and a source of variability in the supply chain. Other funding agencies such as USAID take a different approach to fund disbursal, and buy ACTs directly from manufacturers on behalf of endemic countries. This approach reduces the amount of involvement from the national buyer, but involves fewer transactions and monetary flows.

**Box 1**

**Supply Side Facilitators** play the important role of funding late-stage research, providing information pertaining to long term market potential, funding clinical trials, helping the manufacturers to obtain better rates from Contract Research Organizations (e.g. Quintiles) and facilitating relationship of smaller manufacturers with international regulatory and technical organizations such as the WHO and national health and regulatory authorities. Examples of supply side facilitators in the ACT supply chain include MMV, DNDI, and One World Health.

**Drug Substance Value Chain** is the process involving the production of Active Pharmaceutical Ingredient (API) and other drug substances required for manufacturing the end product. In the case of Coartem, this value chain consists of Artemisia growers, artemisinin extractors and API producers.

**Manufacturers** are responsible for the production and sale of ACTs to the mass market. Qualified manufacturers, e.g. Novartis and Sanofi-Aventis have products that are PIC/S approved, and non-qualified manufacturers, e.g. Dafra, Ajanta Pharma currently do not have PIC/S approval for their products.

**Quality Regulators**, e.g. the WHO, FDA, EMEA, and PIC/S, are responsible for ensuring the quality of the drug. In this category, we also consider internal quality standards of funding agencies that guide which manufacturer recipient countries can buy from. In addition to being approved by a quality regulator, many buying countries have their own national registration process in which drugs must be registered by a national entity.

**Global Technical Agencies**, e.g. the WHO, are responsible for setting treatment norms and guidelines.

**Funding Agencies**, e.g. the World Bank, GFATM, and USAID, give grants and loans to malaria control programs.

**Donors** are comprised of countries, like the UK Government, and philanthropic foundations, like the Gates Foundation, that give money to funding agencies.

**Procurement Agents,** e.g. IAPSO, UNICEF, and the WHO assist countries in ordering and purchasing ACTs.

**Logistics Providers**, such as JSI Deliver, handle shipping and transport of ACTs from the manufacturer to the buying country, and assist in distributing it throughout the buying country.

**National Public Buyers,** e.g. the Ministry of Health, are the government entities responsible for purchasing ACTs for the public sector.

**Aggregate Demand Forecasters**, e.g. RBM (MMSS) are responsible for determining the demand forecast for ACTs on a global level

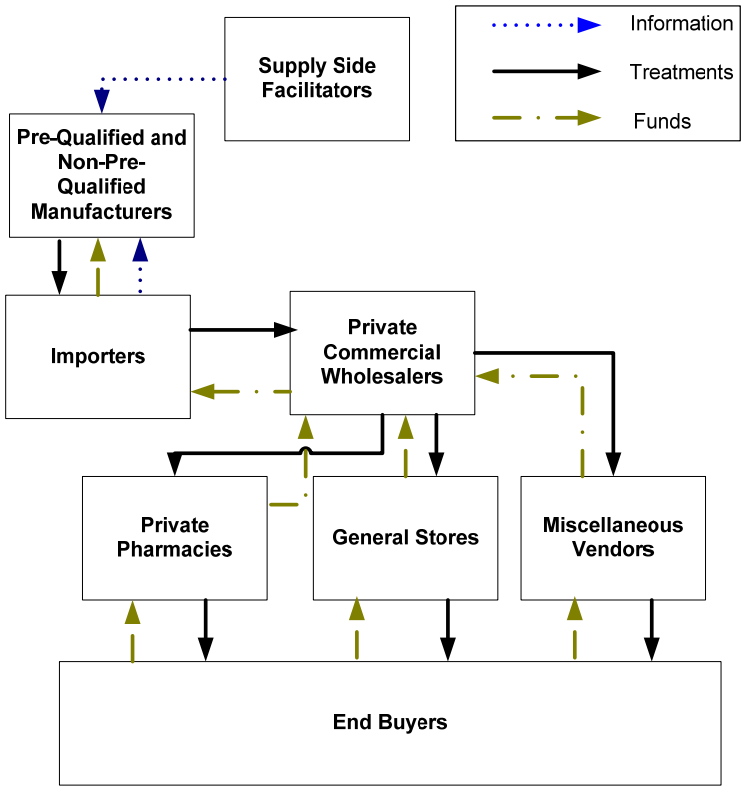



**Figure 3: Stake holders and flows in the ACT supply chain (typical private sector)**
Developed from: CHAI Study 2006 and Arrow et al 2004.

The purchasing and distribution of ACTs follows different processes in the private and the public sector as shown in Figures 2 and 3. We observe that there are fewer monetary flows and much clearer information flows in the case of the private sector. Admittedly, in the private sector ACTs are reaching their intended markets in a timely way. The problem, however, is that only a small fraction of the affected population can afford its ACTs through the private sector. Not only are ACTs for private sector priced higher by the manufacturer, but the markups that each intermediary places on the drug result in a much higher price for the end buyer.

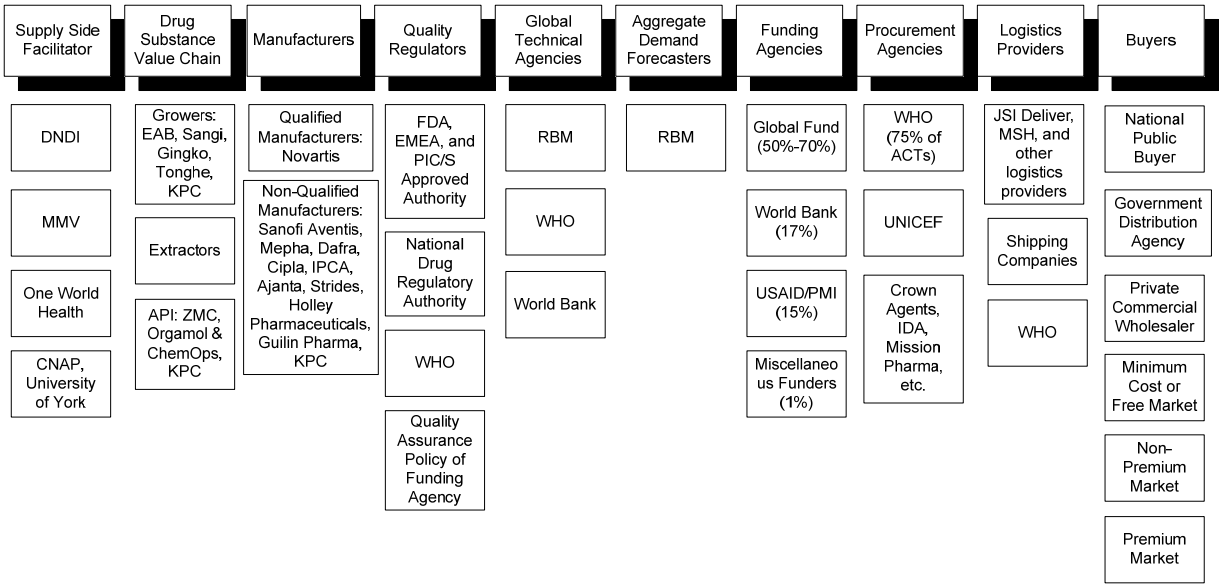



**Figure 4: Stake holder map of the ACT supply chain (circa June 2006)**

Our analysis suggests that the landscape of this already complex value chain is likely to see a major change in the immediate future. The following figure represents our best estimate of who will be future stakeholders in the supply chain.

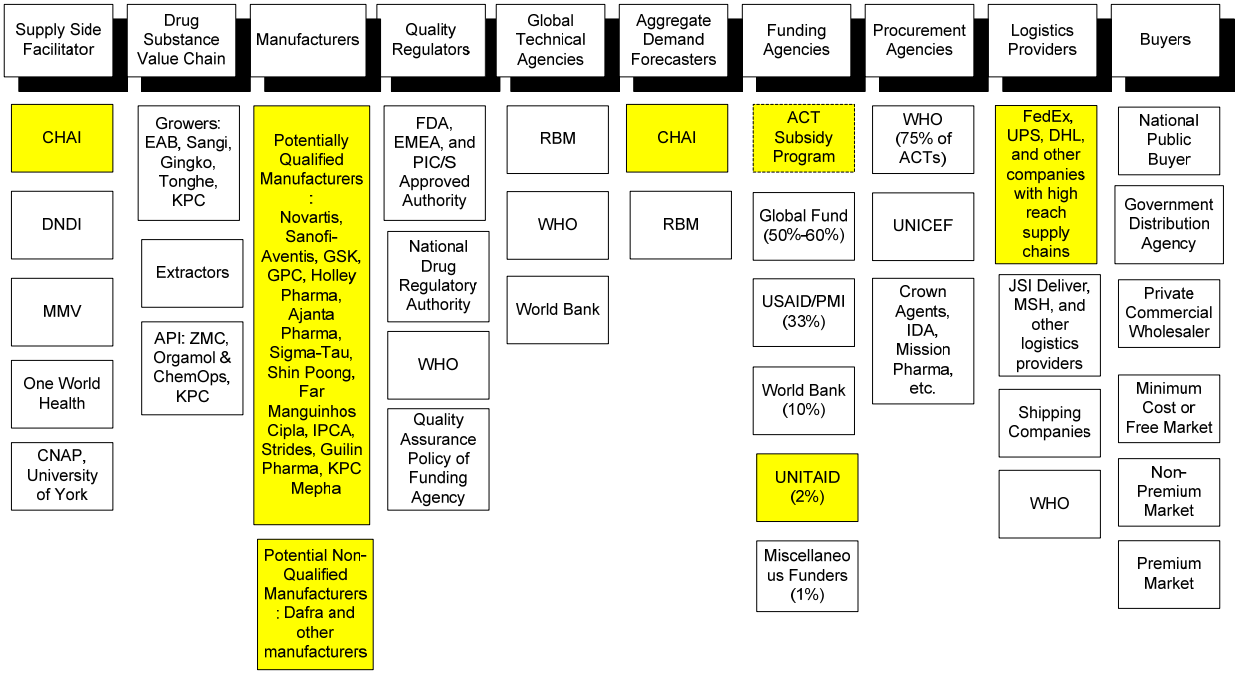



**Figure 5: Projected stake holder map of the ACT supply chain**

While we are predicting numerous changes throughout the supply chain, we feel the need to highlight three crucial changes: an increase in the number of manufacturers, an increase in the number of funding agencies and an increase in the number of procurement agents.

Currently, Novartis is the only pre-qualified co-formulated ACT manufacturer. However, there are numerous manufacturers with ACTs in the pipeline, and we expect this to have a large impact on the ACT market.

**Table 4. Drug Pipeline for ACTs**
*Sources: DNDi, MMV, CHAI, WHO*

| Supplier | Type of Drug | Status/Remarks |
|---|---|---|
| Mepha | AS/MQ | NDRA Approval<br>Pre-Qual applied in 2003 |
| IPCA | AR/AQ | Pre-Qual applied 2004 |
| Ajanta Pharma | AL | Pre-Qual for Generic Coartem applied in May 2006 |
| Holley Pharma+<br>Sigma-Tau | DHA+<br>Piperaquine | Artekin<br>Pre-Qual applied Nov 2004 |
| Sanofi-Aventis | AS/AQ | Pre-Qual applied ? |
| GSK | CDA | Artemesinin combination of LapDap<br>At the advanced clinicals stage |
| Shin Poong | Pyronaridine/AS | Advanced clinical trial stage |
| Far Manguinhos | AS/MQ (FDC) | DNDi partnered project in Clinical Trials |

Some argue that the increase in the number of manufacturers will benefit the end user because as competition increases, the price at which ACT will be sold will decrease. Additionally, with the increase in players, any improvements or innovations in best-practices could extend the efficiency frontier. As it stands today, Novartis has the capacity of producing 120 million treatments per year, and is currently utilizing approximately 50% of this capacity. With new manufacturers entering the market, the overall ACT capacity will be increased; yet fixed asset utilization for each manufacturer will be lower unless aggregate ACT demand increases substantially. Without this increase in demand, costs for manufacturers may go up.

In addition to qualified manufacturers, we expect an increase in the amount of ACTs that will be produced by non-qualified manufacturers with poor or undocumented GMP records. This could impact the market by flooding it with substandard quality products, which in turn could compromise the perceived efficacy of ACTs and possibly jeopardize the sustainability for ACT treatments in the long term.

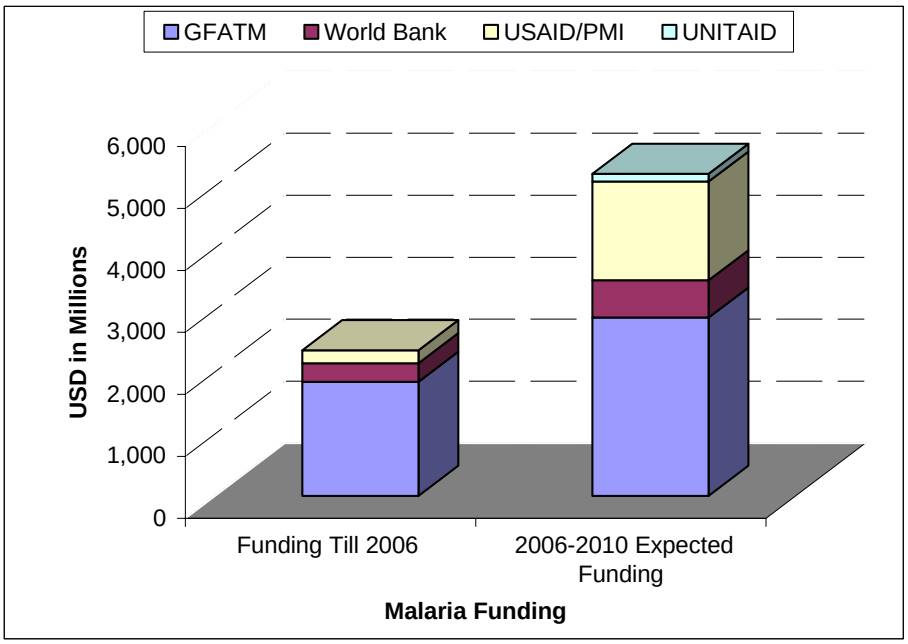



**Figure 6: Historical and Projected Funding Levels and Sources of Malaria Funding**
Source: Estimates received from GFTAM, USAID, World Bank and UNITAID

While we see the increase in funding as a positive sign for the fight against malaria, it is important to address the challenges associated with this growing sector (See Figure 6). As seen in the stake holder map presented in Figure 2, although the majority of funds are channeled through one funding agency, the monetary flow is complex. As the number of funding agencies increase, monetary flows will become more complicated. Furthermore, a unified funding arena, in which buying countries might see the sustainability of funds, will become very fragmented. Also, if each funding agency has a different grant approval process, the transaction cost for grant seeking countries would be higher if they tried to obtain funds from more than one agency. Overall, the increase in funding agencies will create an even more complicated and unclear process.

Currently, even though 75% of ACT procurement is handled by a single procurement agent, i.e. the WHO, there is a large mismatch between supply and demand in the public sector. Manufacturers are uncertain as to the amount of ACTs needed for short term production, and long term aggregate forecasts are anything but precise. In a scenario where many buyers are using different procurement agents, who in turn are placing orders with different manufacturers, two negative consequences can occur. First, because information is fragmented, the level of demand uncertainty will almost certainly increase unless the way in which information is conveyed to manufacturers can be aggregated. Secondly, economies of scale in transaction costs are lost, which can lead to an increase in the procurement costs incurred by each country.

# 4 | Supply Chain Risk Map

The effectiveness and long-term viability of a supply chain is determined by the sharing of risk and reward among supply chain participants. Improper risk sharing leads to the misalignment of incentives and results in sub-optimal behavior of the system as a whole. In this section we first characterize the various types of risks in the supply chain for global health products and then analyze to what extent the supply chain constituents are currently sharing these risks.

Risk in traditional supply chains can be classified into two distinct categories: supply side risks and demand side risks. Also of equal importance in the case of global health supply chains are regulatory and safety risks and other risks related to logistics. Inherently, many of these risks are amorphous and cannot be adequately structured as financial risks. Not including such risks in the analysis, however, does not present a clear picture of the incentives in the supply chain. Often, the more visible risks grab the attention of the stakeholders and mitigation strategies are put in place for them while smaller, unquantifiable risks that create the real goal-incongruence in the supply chain are ignored. We conducted quasi-structured interviews with various stake-holders to assess the current allocation of risks in the supply chain. In our interviews we realized that many of these soft-unquantifiable risks present themselves as “reputational risks” for the supply chain constituents and influence their decision making. We therefore sub-categorize certain important risks as financial and reputational risks. We define reputational risk as the impact that negative publicity can have on an institution's future e.g. decline in future revenues or donor funding, reduction in the customer base, costly litigation or restructuring to take away authority over a function.. The risks we analyze are defined in the accompanying box.

**Box 2**

**Supply-Side Risks**

**Batch Yield Risk**: Pharmaceutical production typically occurs in batches and each production batch has a probability of being rejected due to quality problems. Rejection of a batch results in loss of the value invested in the pharmaceutical intermediates and the drug product production itself. Risks such as harvest yield uncertainty of Artemisia are also categorized as batch yield risks.

**Excess Inventory Risk:** If the demand up-take of a product deviates strongly from the forecast, there is a risk of carrying excess inventory in the supply chain. In the case of short shelf-life products, this risk manifests itself as the cost burden of inventory write-offs. In other products, it is the financial cost of carrying inventory for a long period of time. API manufacturers or pharmaceutical companies that use flexible manufacturing capacity also incur an opportunity cost of not utilizing their flexible resources for the production of an alternative product.

**Long Term Over-Capacity Risk:** Pharmaceutical companies and API manufacturers build production capacity based on long term forecasts that are available to them. If these long term forecasts are much higher than the actual demand realized, they bear the risk of making a long term investment that will not break-even or pay-off.

**Shortage risks**: The shortage of a pharmaceutical product can lead to mortality and morbidity in the affected population. There are also simpler financial risks such as loss of profit margin. There is also an immense reputational risk for many players due to the negative publicity that is generated by such shortages.

**Demand-Side Risks**

**Grant Approval and Disbursement Timing Risk:** The uncertainty in the timing of grant approval and disbursement of funds to recipient countries from the funding agencies manifests itself as uncertainty in the realized demand of the product in any given time period.

**Sustainability of Funding**: This risk stems from the uncertainty about the overall level of funding available from the donor organizations and for the endemic countries the uncertainty pertaining to the level of future funding support available from the funding agency to sustain a development program.

**Risk of Price Increase /Risk of Price Decrease**: Risk related to the uncertainty regarding future price of the procured product. Price may end up being higher or lower than expected when key manufacturing or use decisions were made.

**Regulatory and Safety risks**

Counterfeit product in the supply chain could lead to lives lost and also reduces the patient population's perception of the efficacy of the actual drug if they cannot distinguish between the two.

If drugs approved by a regulatory authority are later found to be unsafe this again could lead to lost lives. Similarly, the lack of available drugs to treat a disease also leads to lost lives. These risks manifest themselves mainly as reputational risks. Unpredictable changes in regulatory regime such as inclusion of new requirements is another risk faced by some of the supply chain constituents.

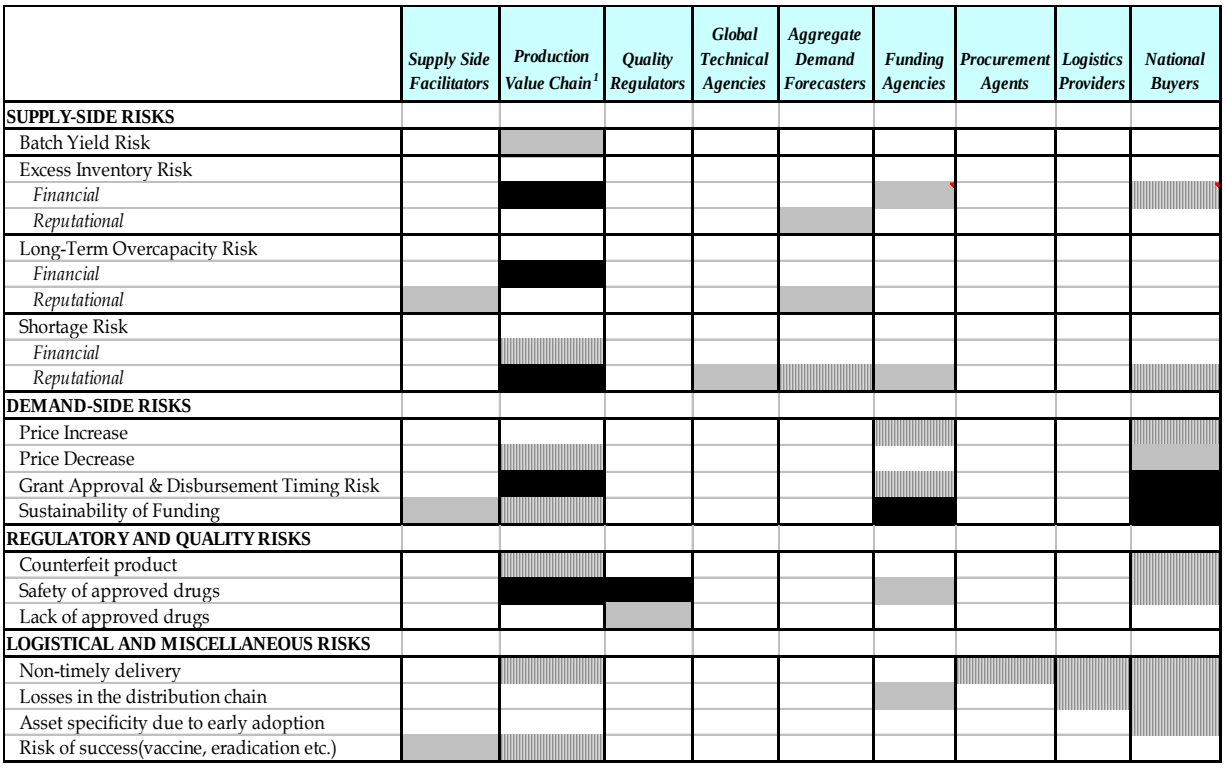
**Logistical and Other Risks**

**Non-timely delivery:** Weaknesses and bottlenecks throughout the supply chain such as long and unreliable transportation lead-times result in stock-outs and lost lives. This is a reputational risk faced by many players involved in the delivery chain.

**Losses in distribution chain –** Uncertainty regarding the velocity of distribution and poor estimates of the available warehousing capacity results in wastes and leakage of product.

**Risk of asset specificity due to early adoption of a product**: If a country changes its treatment guidelines, it involves making investments that are specific to that treatment option. Later if it that treatment option is found not to be the most optimal option, these investments are sunk.

**Risk of success (vaccine, eradication etc.):** The development of a vaccine or the complete eradication of a disease eliminates the raison d'être of some system constituents.




[1] For brevity, the manufacturer and the drug substance value chain are included together and termed as the Production Value Chain in this and subsequent maps.

**Figure 7: Current Allocation of Risks in the ACT Supply Chain**

The map can be read across to see the extent to which each stakeholder bears some of that particular risk, and down, to see which stakeholders are taking the greatest risks in the supply chain. The darker the square, the more that a particular risk is borne by that stakeholder. So for example, in the case of financial risks for excess inventory, manufacturers bear the greatest burden for this risk because in the current contracting arrangements, they do not receive purchase commitments, but must have inventory available to fill orders as they are placed; national buyers bear some risk if they order too much and the excess inventory sits in their warehouses; while funding agencies bear an indirect risk if their monies are ineffectively used, when national buyers over-order and excess inventory results in wastage at the country level.

Looking at the map by stakeholder, a quick glance shows that most of the risks in this supply chain are borne by manufacturers. National buyers also bear some risks, most acutely around sustainability of funding. In some cases, you will note that the risk is lopsided; for example, in the case of quality regulators, they bear a much higher risk if drugs that they approve are later found to be unsafe, than the risk they bear if drugs are not moved expeditiously through the pipeline.

The extent of the risk that each party does or does not bear, and whether these risks are lopsided, will cause a misalignment of incentives in the supply chain, which is discussed in the next section.


| | *Supply Side Facilitators* | *Production Value Chain*[1] | *Quality Regulators* | *Global Technical Agencies* | *Aggregate Demand Forecasters* | *Funding Agencies* | *Procurement Agents* | *Logistics Providers* | *Pharmacies,Hospitals* |
|---|---|---|---|---|---|---|---|---|---|
| **SUPPLY-SIDE RISKS** | | | | | | | | | |
| Batch Yield Risk | | | | | | | | | |
| Excess Inventory Risk | | | | | | | | | |
| *Financial* | | | | | | | | | |
| *Reputational* | | | | | | | | | |
| Long-Term Overcapacity Risk | | | | | | | | | |
| *Financial* | | | | | | | | | |
| *Reputational* | | | | | | | | | |
| Shortage Risk | | | | | | | | | |
| *Financial* | | | | | | | | | |
| *Reputational* | | | | | | | | | |
| **DEMAND-SIDE RISKS** | | | | | | | | | |
| Price Increase | | | | | | | | | |
| Price Decrease | | | | | | | | | |
| Grant Approval & Disbursement Timing Risk | | | | | | | | | |
| Sustainability of Funding | | | | | | | | | |
| **REGULATORY AND QUALITY RISKS** | | | | | | | | | |
| Counterfeit product | | | | | | | | | |
| Safety of approved drugs | | | | | | | | | |
| Lack of approved drugs | | | | | | | | | |
| **LOGISTICAL AND MISCELLANEOUS RISKS** | | | | | | | | | |
| Non-timely delivery | | | | | | | | | |
| Losses in the distribution chain | | | | | | | | | |
| Asset specificity due to early adoption | | | | | | | | | |
| Risk of success(vaccine, eradication etc.) | | | | | | | | | |

**Figure 8: Allocation of Risks in the Pharmaceutical Supply Chain (US)**

As a point of comparison, Figure 8 shows the risk map for a typical pharmaceuticals commercial supply chain in the U.S. In this map it is clear that risks are more evenly distributed among many parties in the supply chain. For example, in the case of the excess inventory risk described above, it is shared between the manufacturer and wholesaler/distributors such as Cardinal Health, McKesson, Amerisource Bergen as well as large pharmacies, which hold inventory in their warehouses. In the case of long term over capacity, there are a variety of organizations that aid in drug commercialization which also invest and share these risks with the primary branded manufacturer. The more even distribution of risks in this supply chain allows it to function more effectively and ultimately, results in better alignment of incentives.

### Conclusions

The distribution of risks in the ACT supply chain indicates that there is considerable opportunity for greater sharing of risks between stakeholders. While the role of wholesaler does not exist in the ACT supply chain, others in this chain, particularly funding agencies, may be able to participate in sharing

more of the risks that are currently borne by manufacturers. If the global community expects suppliers to provide their products at low or no margins, and also guarantee access to products when and where they are needed, then it will be necessary for others in the supply chain to find ways to share some of the risks that the suppliers are currently facing. In the long run, if manufacturers absorb more risk but do not receive higher returns to compensate for this greater risk, they may engage in behaviour that eventually hurts all supply chain constituents.

# 5 | Supply Chain Incentive Audit

Based on the risk map in section 4, an incentives map (Figure 9) was created for the ACT supply chain. This map shows whether each stakeholder has a clear incentive, a clear disincentive or neither, to engage in a particular behaviour.

| | | | |
|---|---|---|---|
| Disincentive | ↓ | Indifferent | - |
| Incentive | ↑ | Potential Misalignment | |

| | *Supply Side Facilitators* | *Production Value Chain* | *Quality Regulators* | *Global Technical Agencies* | *Aggregate Demand Forecasters* | *Funding Agencies* | *Procurement Agents* | *Logistics Providers* | *National Buyers* |
|---|---|---|---|---|---|---|---|---|---|
| **SUPPLY-SIDE** | | | | | | | | | |
| Develop Innovative Products | ↑ | ↑ | - | - | - | - | - | - | - |
| Increase size of the supply market | ↑ | ↓ | - | ↑ | - | ↑ | ↓ | - | ↑ |
| Decrease supply chain lead time | ↑ | - | - | ↑ | - | - | ↑ | - | ↑ |
| Overforecast in the Short-Term(< 12 months) | - | ↓ | - | - | ↑ | ↑ | ↑ | - | ↑ |
| Underforecast in the Short-Term(< 12 months) | - | - | - | - | ↓ | ↓ | ↓ | - | ↓ |
| Overforecast in the Long-Term (1-5 years) | ↑ | ↓ | - | ↑ | - | ↑ | - | - | ↑ |
| Underforecast in the Long-Term (1-5 years) | ↓ | ↓ | - | ↓ | - | ↓ | - | - | ↓ |
| Sharing Information on demand, inventory… | ↑ | ↓ | - | - | ↑ | - | - | - | - |
| **DEMAND-SIDE** | | | | | | | | | |
| Decrease wholesale price of ACTs | ↑ | ↓ | - | ↑ | - | ↑ | - | - | ↑ |
| Decrease retail or end-customer price of ACTs | ↑ | ↑ | - | ↑ | - | ↑ | - | - | - |
| Expedite grant approval and disbursement | - | ↑ | - | - | - | ↑ | - | - | ↑ |
| Rapid adoption of ACTs as a treatment option | ↑ | ↑ | - | ↑ | - | ↑ | - | - | - |
| Enhance the level and sustainability of funding | ↑ | ↑ | - | ↑ | - | ↑ | - | - | ↑ |
| **REGULATORY AND QUALITY** | | | | | | | | | |
| Ensure regulatory compliance and safety | ↑ | ↑ | ↑ | - | - | ↑ | - | - | ↑ |
| Expedite regulatory approval of new drugs | ↑ | ↑ | - | ↑ | - | ↑ | - | - | ↑ |
| **LOGISTICAL AND MISCELLANEOUS** | | | | | | | | | |
| Improve efficiencies in distribution chain | - | - | - | ↑ | - | ↓ | - | ↑ | ↑ |
| Ensure availability of complementary inputs | - | ↓ | - | ↑ | - | ↑ | - | - | ↑ |
| Achieve long lasting success(eradication) | ↑ | - | - | ↑ | - | ↑ | - | - | ↑ |
| Have rigorous accountability in funds usage | - | - | - | - | - | ↑ | - | - | ↓ |

**Figure 9: ACT Supply Chain Incentive Map**

Note that it is not necessarily "good" to have a positive incentive and "bad" to have a disincentive. This depends on how the incentive, disincentive, or lack of incentive affects the main goal of the supply chain, which is to provide access to products. So for example, in the case of long term capacity forecasts, manufacturers' incentives are balanced: they have a disincentive to both over forecast and under forecast because, as we saw in the risk map, they bear the costs of overcapacity; whereas incentives of the national buyers for long term capacity forecasts are lopsided: they have an incentive to over forecast so that they can guarantee capacity from the supplier, but no incentive to under forecast, (which would result in more accurate estimates of demand), because they bear no risks for over capacity.

Significant misalignments in the supply chain are highlighted in gray. The map shows a significant misalignment in short term forecasting. In this case, manufacturers have an incentive to under forecast because they bear the costs of excess inventory while others in the supply chain such as funding agencies, procurement agents, and national buyers have an incentive to over forecast because they bear

very limited risk for excess inventory but want to guarantee access to the product. Ideally, stakeholders should have balanced incentives for under and over forecasting, which would result in more accurate matching of supply and demand. This would require that forecasting risks are more evenly shared among the relevant parties.

Another important area of misalignment is sharing of information on demand and supply (e.g. buyer intentions, inventory levels). The map shows that there is no clear incentive for most players to share information regarding demand and supply with others. In fact, the manufacturers have a disincentive to share information as making their inventory levels public may lead the buyers to be aware of where they can obtain the shortest lead-time, which could imply reduced market share for the manufacturer that has lower in stock availability of a product.

We observe that the quality regulators do not have an incentive to expedite the regulatory approval of new drugs by investing in more capacity or resources. This misalignment can be remedied by creating a system of positive reinforcements for the quality regulators.

Also, notable is the disincentive of the procurement agents to have a market with many suppliers. A procurement agent needs to build relationships with the supplier, create information interfaces, evaluate bids and administer contracts. Hence, the procurement agent prefers a market where its clients can choose only from a very limited set of suppliers thereby decreasing its needs for the activities described above.

We see that manufacturers have a disincentive to decrease the wholesale price of ACTs. If the manufacturers realize that lower wholesale prices will lead to higher sales volumes, they will be willing to forego a high per treatment margins in lieu of higher overall volumes. This requires assurances to the manufacturer that lowered prices necessarily lead to higher volumes in the long-run.

The indifference of the buying countries towards rapid adoption of ACTs and to decrease the retail price of ACTs in the private or public market are another set of misalignments that need to be carefully addressed.

In summary, we see various clear misalignments of incentives in the ACT supply chain. In the next section we present the remedial interventions that are common across many misalignments.

# 6 | Recommendations for Intervention

In this section we present our recommendations to remedy the misalignment of incentives and goal incongruence that arises from incoherent risk sharing. Most of our recommendations are interrelated (at times sequential) and their implementation in isolation may not always be possible, or would atleast require further analysis.

## 6.1 Global Health Infomediary

Opacity of data from the supply chain nodes (manufacturer, funding agency, recipient country, procurement agent) increases demand uncertainty and its associated risks. The pressing need for operational transparency of data at or within supply chain nodes is already acknowledged in global health circles and unlike other recommendations is relatively uncontroversial. Sharing demand forecast information has been recognized as a key element in private sector supply chain coordination. Over the last decade, companies have engaged in forecast and information sharing practices, including the commonly known Collaborative Planning, Forecasting and Replenishment (CPFR) initiative, which was launched to “create collaborative relationships between buyers and sellers through co-managed processes and shared information.” Retailers such as Wal-Mart and Best Buy, along with their suppliers such as Procter & Gamble and Kimberly-Clark, all use CPFR and have reported extremely good benefits.

The advantages of information sharing for better forecasting come from two sources:

- **Diversity of information** that each player has can lead to more accurate overall forecast e.g. the funding agency has better information about the status of procurement plans, the manufacturer knows better about the supply constraints, the procurement agent knows better about the preference of a country for a specific manufacturer, etc.
- In certain instances, when two players, who do not have a high diversity of information, share their forecasts, it leads to a **confirmation effect**. Each player assigns a higher degree of certainty to the forecast, thereby carrying lesser safety inventory in the supply chain.

One of the reasons for the poor adoption of forecast sharing or information sharing in global health supply chains stems from its inherent incentive problems. Clearly, forecasting and analysis is particularly relevant to those who are increasingly affected by the risk of over-forecasting or under-forecasting. Previous analytical research has suggested that the buyer has an incentive to inflate forecasts to assure sufficient supply (Lee et al. 1997), or the buyer under-invests in forecasting related activities(Yadav and Schmidt 2005). Similarly, in order to obtain high levels of product availability and a stronger supply market, funding agencies and the recipient countries may have an incentive to overstate the forecast and the manufacturer, in the short-run, may want to under forecast to avoid excessive short-term inventory risks.

If forecasts are successively inflated, they will be rationally ignored by the producer as we may have seen in the case of one of the manufacturers of ACTs. Similarly, in a market with many manufacturers, the manufacturers' incentives to share their current inventory information are also diminished as advanced knowledge of low stocking levels to the buyers may lead to decreased market-share. In addition, Davenport (1992) cites *information culture* and *information politics* as the main hurdles to information sharing within and across organizational boundaries. Such and many other issues not presented in detail in this report prohibit the multi-party exchange of information in this supply chain.

We therefore recommend the creation of an agency for the brokering and intermediation of information in the global health supply chain. We choose to term such an agency an *infomediary* (information intermediary).

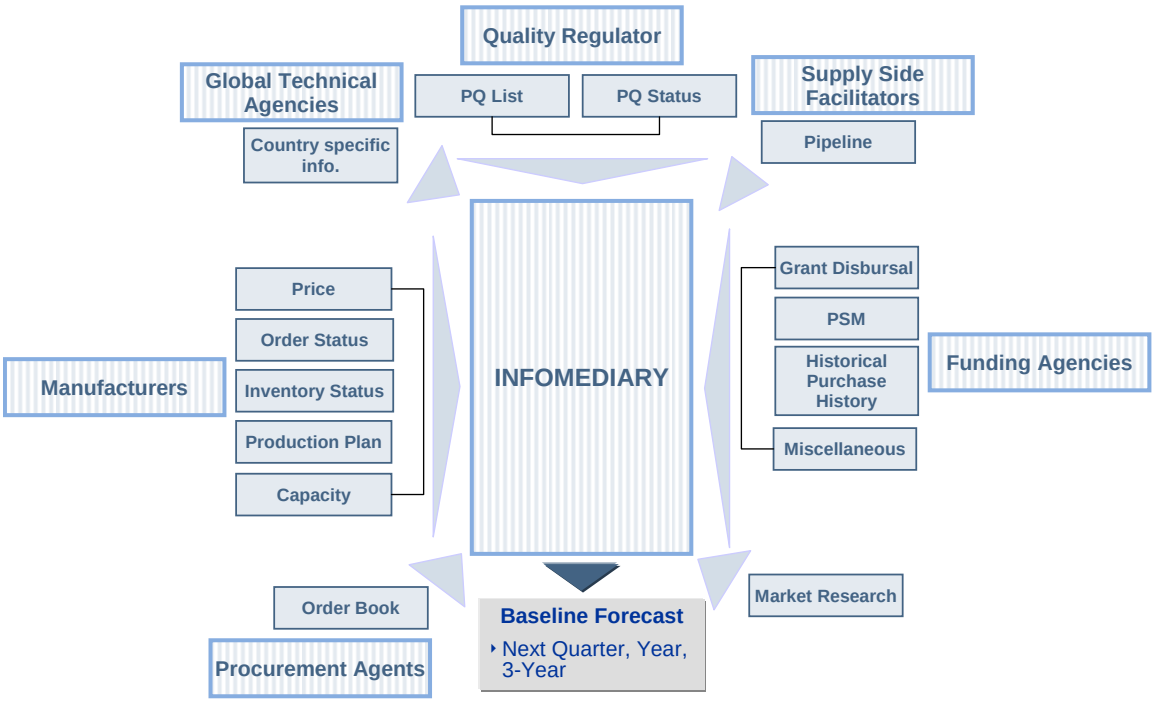



**Figure 10: Schematic of a Global Health Infomediary**

The infomediary will play a three-fold role:

1. It will act as central repository of all relevant demand and supply data.
2. It will conduct periodic market research for different product categories based on extrapolation from a pre-defined sample of public-sector and private sector buyers.
3. It will generate baseline aggregate forecasts (by category) based on the information sets provided by as inputs from various sources.

Naturally, all parties may not choose to work with the baseline aggregate forecast and instead create their own forecast adjustments to the base-line. Individual manufacturers would estimate the forecasted volumes for their products based on the projected market shares and the aggregate category level forecast.

The infomediary shall only carry out the task of *demand anticipation*. The roles of *demand stimulation* and *demand fulfillment* would, however, by careful design not be included in the role of the infomediary as that may create a potential incentive problem.

Pharmaceutical companies extensively rely on data from organizations such as IMS Health for therapeutic category demand history and projections, inventory in pipeline and PBM/hospital formulary status. In grocery products, music and books, independent data collection companies such as IRI or Nielsen collect and broker this type of data.

It is not pragmatic to assume that all constituents will agree to share all of the information sets outlined in Figure 11 with the infomediary. In fact, the reluctance to share is quite rational, on account of fears of weakening their bargaining power, competitive position and revealing performance data, etc. To alleviate such concerns, a secure sharing arrangement can be setup such that such information collaboration can take place without revealing any participant specific data to the others.

The infomediary will work based on a fee-for-service model under which some constituents or a donor will pay an annual base fee to the infomediary. A clear pay-for-performance fee structure will be established such that the member constituents will pay a higher fee as the aggregate baseline forecast performance improves.

The question remains, does this require the creation of a new entity, or can it operate within an existing global health organization. Does it need to be a third party agency necessarily or can one of the existing constituents play that role? This report does not take a position on the specific entity that would be best able to fill the role of an infomediary. However, we do recommend that it would be ideal if the infomediary role was played by an established organization with sufficient capacity and experience in the following areas:

- Multi-Party and Multi-Level Data Aggregation and Information Management
- Developing Country Health Markets
- Advanced Analytics
- Global Market Research
- Supply Chain Management: Inventory and Order Flow Tracking

## 6.2 Risk sharing mechanisms

Next we focus on measures that more explicitly share risks and their corresponding rewards between supply chain partners. Each risk sharing mechanism comes with a transaction cost. We attempt to identify solutions with reduced risk sharing transactions cost. Also, different risk sharing mechanisms will have varying impact on the behavior of the parties involved, risks imposed on them, and the resulting supply chain efficiencies. An important element of our approach is the transfer of excessive risk and any accompanying rewards from the manufacturer to the funding agencies. This hinges on the assumption that given an adequate potential for positive reward, funding agencies will also become partial risk absorbing agencies. In the following paragraphs, we first present the economic rationale for transferring some of the risks to the funding agencies and then describe an operational way of doing this through rolling horizon forecast commitments.

**Risk allocation rationale**

Based on our earlier research and standard economics principles, we argue that the constituent that has:

- the best knowledge about an uncertain event (in this case the timing and quantity of orders) , or
- the highest ability to (partially) resolve the uncertainty regarding the uncertain event , or
- the highest potential benefit from the uncertainty reduction;

needs to carry some of its corresponding risk.

Long term demand variability can be reduced by efficient grant disbursals, more stringent requirement for adherence to the time-lines in the procurement plans from the recipient countries and creating additional incentives for countries that procure drugs in a timely and scheduled manner (See figure 11). Each of these levers for reducing demand variability is influenced by the funding agencies. Admittedly, the funding agencies themselves alone cannot directly resolve a large part of this uncertainty as it stems from a myriad of complex interactions that happen at the country level after a grant disbursal. However, they are able to assert their leverage on the recipient countries to reduce some of this uncertainty.

Currently, the manufacturers undertake a large portion of the risks associated with long term and short term demand uncertainty. The manufacturers' risk due to long term demand uncertainty would result in higher production costs in the long-run (or at the very least will prohibit any decreases in the manufacturing cost). A higher volatility in demand implies a higher likelihood that the manufacturers or drug substance producers would be stuck with large inventory excesses at the end of a planning period. This leads them to choosing smaller production campaign sizes resulting in higher manufacturing costs as the economies of scale do not set in. These higher manufacturing costs are passed on to the buyer, who is in turn being financed by the funding agency. Thus, in the end this long term demand uncertainty results in a higher drug procurement cash outflow for the funding agency.

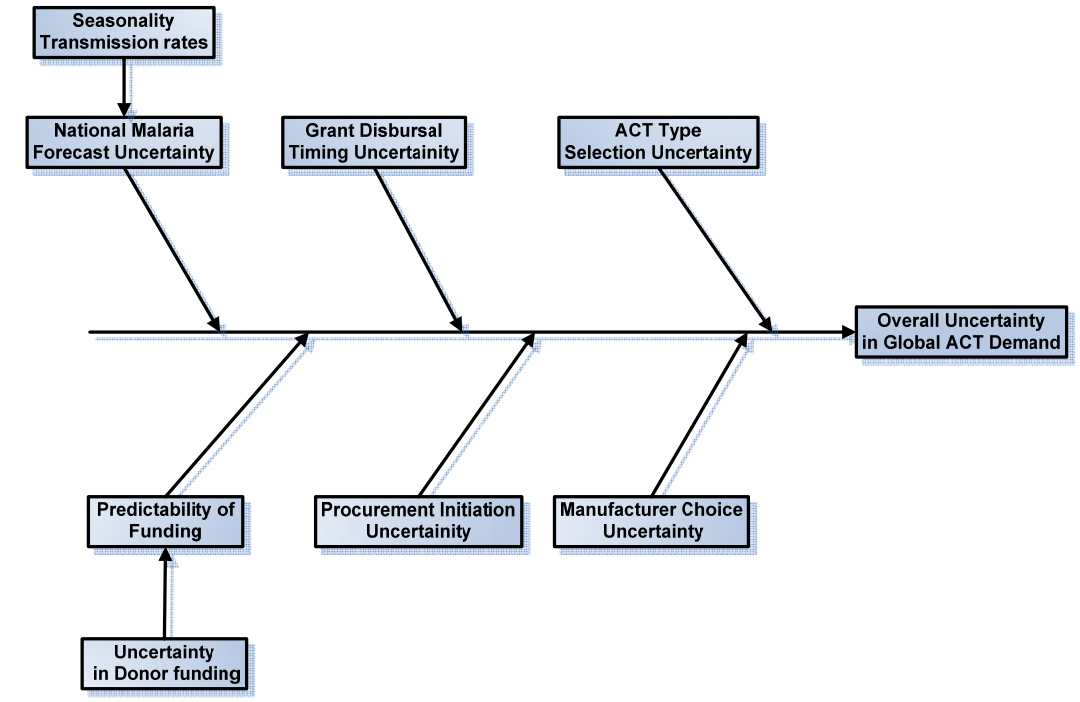



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**Figure 11: Sources of Demand Uncertainty in the ACT supply chain**

This shows that an optimal allocation of the risk owing to the long term demand uncertainty would involve transferring some portion of this risk to the funding agencies. We propose to achieve this risk transfer through rolling horizon forecast commitments from the funding agencies to the manufacturers.

**Rolling Horizon Forecast Commitments**

Market incentives such as *advanced purchasing commitments* have been traditionally used to incentivize manufacturers to develop and commercialize drugs for diseases with limited market potential. The *rolling horizon forecast commitment* structure we propose is similar in basic nature and transfers some of the long term excess inventory risk to the funding agencies. This is, however, an operational risk-transfer mechanism and not a market-making mechanism as is the case with advanced purchasing commitments. This mechanism provides the funding agencies with a high level of long term and low level of medium term flexibility. The short term risk is still carried mostly by the manufacturer or is partially mitigated through the use of pull-supply chains as described later in this report.

In essence, the rolling horizon forecast commitment requires that the funding agencies provide the manufacturers with commitments to purchase a certain quantity of the product in each of the following three years with some flexibility on updating the commitment as new information becomes available. In return for the flexible purchase commitments, the manufacturers have to guarantee the funding agencies a maximum allowed lead-time, up-side purchase flexibility and low acquisition cost. Explicit contractual penalties are defined for the manufacturer if it is not able to meet either its lead-time commitment or the

up-side supply guarantee. Thus, the funding agency reduces its risk of supply shortage and price uncertainty by undertaking some of the demand uncertainty risk. This is clearly a rational allocation of risks: the manufacturers control price and supply and hence undertake those risks, and the funding agencies have the most influence over levers to reduce demand uncertainty and hence undertake those risks. By incorporating an appropriately chosen flexibility parameter in the purchase commitments, we can also strike a balance between the extent of risk faced by the manufacturers and the funding agencies.

We illustrate our proposed rolling horizon forecast commitment mechanism with a simple example below:

Imagine in 2007, the funding agency provides the manufacturer with an advanced partially flexible commitment to purchase 100 units in the year 2010. In 2008, the funding agency has the flexibility of updating its earlier commitment of 100 units by +/-20%. Based on new forecast information, the funding agency can update its purchase commitment to be anywhere between 80 and 120. Let us say that the funding agency has new information to conclude that some of the orders slated to be placed in 2010 will now be placed in later years. It will revise its earlier commitment of 100 and choose a new commitment for 2010 as 90 units. In 2009, the funding agency (as it learns more precise information about quantity and timing of order placement) has the ability to further update its earlier estimate of 90 units for 2010 by +/- 10%, so the new commitment could be between 81 and 99. Assume it chooses to commit for only 85 units. At the start of Year 2010, the funding agency has one last chance to change its estimate by +/- 5% and therefore can now choose any quantity between 80 and 89 which will then become its firm commitment to purchase. The manufacturer will however provide a guarantee of the availability of 89 units within a 3 week lead-time. Figure 12 illustrates this example arrangement graphically.

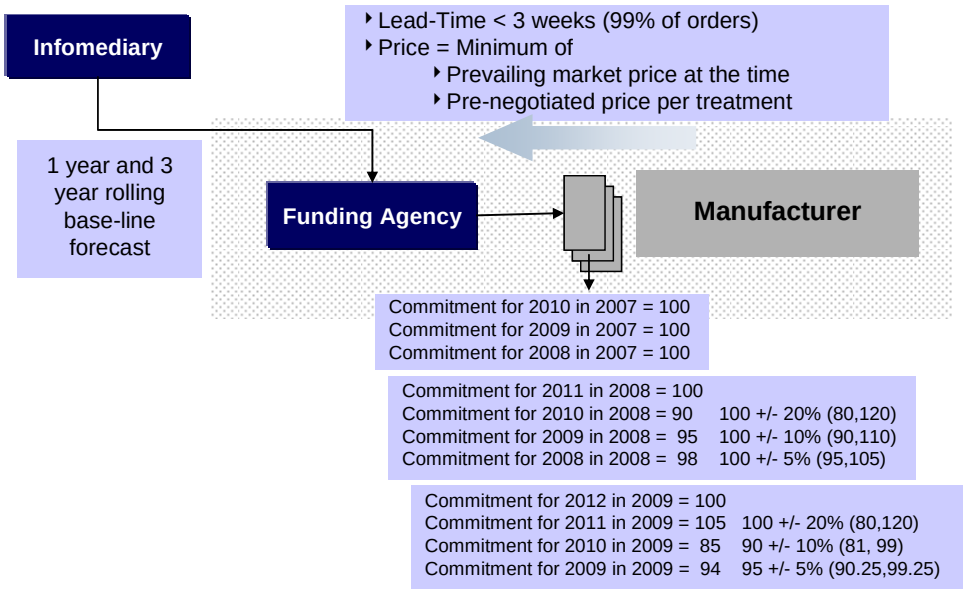


**Figure 12: A simple example of the risk sharing arrangement in rolling horizon**

Flexibility % and other numbers are chosen only for illustrative purposes and their exact determination requires a thorough analysis of the forecast certainty, risk aversion ability etc.

The level of flexibility in the commitments at each stage and any contractual penalties for not meeting the guaranteed lead-times need to be chosen carefully based on a thorough analysis of the forecast certainty, risk aversion ability etc. The exact timing of the placement of orders within the year is a risk that the manufacturer continues to undertake as before although our concept of demand-driven supply network as in the following sections attempts to minimize some of this risk.

Several examples of the use of such contract exist in electronics and telecommunication equipment supply chains, and one of the authors has been involved in one such engagement. A rigorous mathematical analysis of rolling horizon forecast commitments can be found in Anupindi and Bassok (1999).

In summary, having the partial onus of long-term overage risk will incentivize the funding agencies to adopt stricter policies regarding timely procurement by the recipient countries and allocate sufficient amounts in the early stage grants to build an agile procurement organization within the recipient countries.

**Framework contracts with manufacturers**

For the rolling horizon forecast commitments to succeed, the funding agency should have some degree of control over the procurement activity of the recipient. This could occur through one of the two proposed methods. Either the funding agency creates “framework contracts” with manufacturers, under which recipient countries can purchase at better terms and the funding agency can make direct payments to the manufacturer, or through pooled purchasing where the funding agency (or its outsourced partner) actually carries out procurement on behalf of the recipient country. Both come with their own set of advantages and disadvantages.

To obtain better insights we need to classify improvements in procurement efficiency into three broad categories: *process efficiency*, *bargaining efficiency* and *information efficiency* (Wang and Yadav 2005). ***Process efficiency*** gains results from the streamlining of purchasing processes when procurement is carried out by an organization with more experience and staffed with people who, because of the sheer volumes they purchase, become more efficient and have better market knowledge. There are clear reductions in administrative and transactions costs, and in some instances the time and quality of some of the steps involved also improves. ***Bargaining efficiency*** gains result from leveraging volume to increase buying power and reduce purchase price. An increase in buying power is also achieved by locating new qualified sources of supply, leading to greater competition in the market. ***Information efficiency*** gains result from the buyers pooling their information about quantity and time of purchase and communicating this to the supply network so that they can all benefit from the reduction in uncertainty due to information pooling.

Bargaining efficiency gains are extremely important in markets where there is a high degree of price volatility and quantity dependent pricing is common. Price volatility in the ACT market is not high and there is, in fact, a high degree of price transparency owing to price reporting initiatives such as the GFATM's GPRM. Thus, the potential of bargaining efficiency gains are minimal. Similarly the gains from information efficiency will be realized for the most part if the infomediary as described before plays its role successfully. The key opportunities for efficiency in this case are thus from process efficiency, rather than bargaining or information efficiency. We argue in favor of a procurement model where the funding agency creates framework contracts with leading manufacturers and the actual procurement function is still carried out by either the recipient country or its chosen procurement agent. This allows the recipient country to retain higher ownership of their malaria programs and provides greater incentives for them to make the micro-level distribution of ACTs successful. These framework contracts should be designed such that the funding agency directly pays the purchase amount to the manufacturers. There are two sources for significant delays as we have found in the procurement processes of the recipient countries: the delays due to multiple to-and -fro monetary flows and the delays in the tendering process itself. Direct payment mechanism significantly reduces the first part and may also indirectly speed up the second.

By setting up these framework contracts, the funding agency would play the role similar to a Pharmacy Benefit Manager (PBM) in commercial pharmaceutical supply chains. Although PBMs do not directly make purchases on behalf of the plan sponsor or health insurer, but they use formularies to obtain deep discounts and supply guarantees from pharmaceutical manufacturers. The role of PBMs in the pharmaceutical value chains has expanded in the recent years, and many health insurers now have their own PBMs. A similar structure appears to be evolving in the global health supply chains.

**Global Health Channel Maestro**

The global health supply chains need someone to play the role of a *channel maestro* who orchestrates the various constituents in this complex network. In the apparel industry, for example, supply chains are very fragmented and have many firms playing different albeit equally important roles. Typically, one constituent takes the role of coordinating the chain and is the channel maestro. In many instances, third party companies such as Lee & Fung play this role. They purchase production capacity on behalf of their many clients at various sites across the globe without clear knowledge of the demand for the upcoming season. Currently, it appears that such a role is not clearly defined in global health supply chains. Also, we note that the agency that plays this role should have the willingness and ability to absorb some risks. Our recommendation of risk transfer to the funding agencies and the setting up of framework contracts for procurement is one step in the direction of extending the channel maestro role for global health supply chains to the funding agencies (or their consortium).

## 6.3 Demand Driven Supply Hub

The risks due to variance in long term forecast can be reduced through better information sharing, and they can be better allocated across supply chain constituents as described in the previous section. The timing of order placement within a year is still a random event that is extremely difficult to predict. Given that the manufacturers will have to guarantee a preset service level to the funding agencies in return for a forecast commitment, the manufacturers will have to carry inventory to buffer against the short term demand variability. This inventory is currently carried by the manufacturer to meet the short-term forecasts that they generate internally. The role of generating these short-term forecasts will continue to be played by the manufacturers. We however suggest a measure that would lead to lesser reliance on forecasts and a higher reliance on actual demand pull.

Activities within a supply chain can be classified as *push* and *pull* depending on whether they are carried out based on a forecast or they are carried out based on observing system status. Under this classification, building inventory based on a forecast of future demand would be termed as a strictly push activity, and replenishing a preset inventory level based on observing its depletion status would be termed as a pull activity. Admittedly, many sub-networks of the physical supply chain operate in a hybrid push and pull mode. In such cases, often times it is advantageous to characterize the *inventory/order interface* or the *push-pull boundary* of a supply chain, i.e. the point at which push and pull processes intersect. We believe that currently the ACT supply chain largely operates in a push mode (Figure 13).

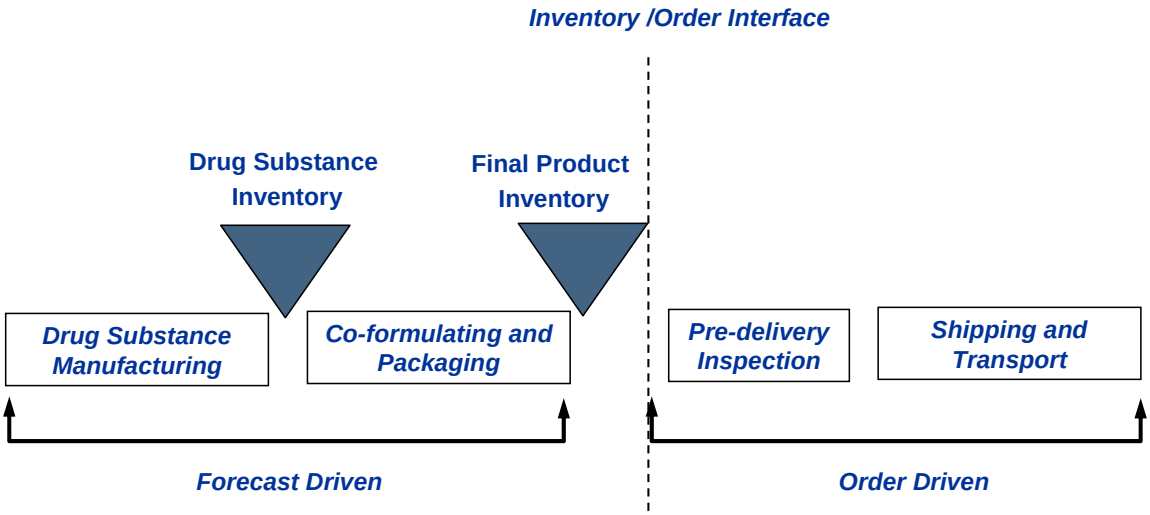


**Figure 13: Forecast-driven and order-driven activities in the supply chain for ACTs**

Given that the manufacturing lead-time is 14 months and the order-lead times are of the order of a few months, it is clear that the manufacturers currently carry a carefully determined physical stock of ACTs in their warehouses. The initiatives to reduce the manufacturing lead-time by use of synthetically developed artemisinin would shift the push-pull boundary of the supply chain to the left, making it more order-driven instead of forecast driven. In addition, we should also attempt to reduce the delivery lead time after orders

are placed. We know that ACTs currently have a very short shelf-life of roughly 2 years, and therefore we should attempt for the quickest possible delivery of ACTs from manufacturers to recipient countries.

We envision a model where the manufacturers, instead of holding inventory to buffer against short term demand uncertainty in their own warehouses, maintain a pre-selected level of inventory in a single third-party warehouse which we term as the *supply hub*. This supply hub co-locates inventory from various qualified manufacturers and is chosen to be in a region that provides quick and easy logistical access to the malaria endemic countries. This reduces the delivery lead-time for any orders placed.

The manufacturers would replenish the stocks at the supply hub as they see actual orders depleting their stock (demand-driven). This implies that a higher fraction of the supply chain will be based on observing the demand status and not on a forecast alone, thereby shifting the push-pull boundary but without necessarily leading to more of the activities starting after the order is received. To avoid any contractual penalties stipulated in the rolling horizon forecast commitment, the manufacturers will continue to hold inventory. On the other hand, since shelf-lives are short, holding excess inventories will be expensive for the manufacturer. These two forces will together incentivize the manufacturers not to under-forecast and to share information. The fine balance required to match supply with demand in the short-run will thus be created. Also, co-located inventory can lead to better preparedness for any time-sensitive short-term demand shock that may require combining more than one source of supply.

The operation of this supply hub should either be outsourced to a third-party logistics company such as UPS, DHL etc. or an agency such as IDPF could include this in its domain.

Two important questions still remain unanswered: 1) who bears any additional cost of transportation due to the centralized supply hub and 2) would it create any tax/duty implications? It is beyond the scope of this report to answer these questions in detail as it requires analyzing the various costs involved.

Also, a unified standard/code for pre-delivery inspection needs to be created and implemented. This will allow unnecessary delays in the delivery after receiving the order. We need to explore if having a unified code can imply that pre-inspected stock is inventoried in the supply hub.

## 6.4 Private-sector Interventions and the Global Subsidy for ACTs

50-70% of malaria treatments are distributed through the private sector (CHAI Study 2006). Thus policy interventions in the public sector market may not have much impact unless we can also attempt to improve the issues and roadblocks in the private sector market. The ACT global subsidy is one such measure that is being contemplated by the World Bank and UNITAID (for details refer to Arrow et al 2004 and Laxminarayan et al 2005). It involves subsidizing ACTs at a much higher level most likely at the manufacturer's factory-gate level. Below we present areas where we see that the ACT subsidy may

crowd out the desired incentives and create further misalignments. This is not intended to be a critique of the ACT subsidy, but we recommend that a comprehensive discussion of these issues should be undertaken before institutionalizing the ACT global subsidy as a policy measure.

- The buying patterns of the endemic countries will change sub-optimally as their cost of overage will be significantly reduced. Currently, if an endemic country buys more drugs than it can distribute, it will incur a huge financial loss (even though the original source of the finance was an aid grant). With heavily subsidized ACTs, the excess versus shortage risk structure of the buying countries will become highly asymmetric and they will not have the incentive to choose the right procurement quantities. Also, their incentives to accurately forecast ACT demand within their respective countries will be further dampened.
- The subsidy is based on assuming that the price elasticity of demand will force the players in the downstream echelons of the supply chain (private wholesaler, general stores and pharmacies) to pass on the benefits of the subsidy to the end customer. This requires a through investigation of whether the high prices of ACT in the private sector are due to a *scarcity premium* or due to rational margin taking at each intermediary level.
- Low-priced ACTs could dampen incentives to optimally allocate the funds for malaria for the endemic countries. As an example, the use of diagnostic tests and ITNs will suffer and hence the overall goal of malaria eradication could be hindered. Empirical evidence shows that the optimal allocation of funds in the case of malaria can yield quick and significant benefits.
- If ACTs become as inexpensive to consumers as CQ treatments, patients whose clinical illness is not malaria will start taking ACTs as has been shown to be the case with CQ treatments. Overuse could then result in earlier development of resistance towards ACTs.
- Additionally, the presence of a global subsidy may create a permanent market distortion in the global health market.

Our analysis suggests that the public buyers have no clear incentives to reduce the retail prices of ACTs (Figure 9). Other measures should be explored for setting and maintaining a ceiling on the retail price for ACTs. Private manufacturers often engage in informal retail price maintenance (RPM) contracts with their retailers or wholesaler wherein they guarantee some “development funds” to the retailer/wholesaler if they keep the retail prices higher (minimum RPM) or lower (maximum RPM) than a specified price. Although these contracts have been controversial and hence not very publicized, it is worth exploring what kind of creative retail price control mechanisms have been used in private industry and if any of those can be successfully utilized in the global heath arena.

## 6.5 Incentives for rapid adoption of ACTs

Malaria-endemic countries find it difficult to modify their malaria treatment policies very rapidly. A change in treatment policy results in costs associated with retraining health workers, printing material that explains new dosing regimes, restocking new drugs, and so forth, which are significant in the malaria budget of a developing country. There are also costs associated with supplier identification and forging relationships with new suppliers (of ACTs). The funding agency grants should allow greater sharing of some of these costs.

Inflows of CQ and traditional treatments occur at different downstream nodes in the distribution chain at the country level. The local CQ manufacturers can ensure deliveries to different geographical location and make shipments to regional distribution warehouses of the countries public health system. When making the switch to ACTs the ex-factory shipment terms and deliveries from a foreign supplier to a single destination increase the distribution burden of the buying country. Building additional infrastructure for this added layer of distribution requires longer term commitment from the global health community towards ACTs.

Approximately 4-6 months of shelf life is already consumed by the time a country receives delivery from a manufacturer. Thus, roughly only 18 months of shelf life is left for distribution within the country (CHAI Study 2006). This risk needs to be shared with the country more implicitly, although we do not present any specific operational models here.

The limitations of time did not allow us to address all the incentive misalignments with appropriate remedial measures. Neither could we operationally validate all our recommendations with experts within those organizations which will require making internal re-adjustments for these recommendations to be feasible. However, at the very minimum, this report presents a new way of looking at the issues in global heath supply chains. The framework presented here can be utilized for the supply chains of various other global health products and it is our opinion that many of these recommendations are also, in-principle, applicable to other global health products.

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