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A Value for Money Perspective Applied to Global Health Initiative Market Shaping Activities

Final Report

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Executive Summary

In the past decade, the global architecture around access to medicines for neglected diseases has changed, in particular with the rise of Global Health Initiatives (GHIs) as major sources of health technology funding. However, our knowledge of the impact of GHIs on access to medicines, as an essential part of functioning health systems, is limited. The Lancet paper written by the Positive Synergies Collaborative Group[1] had little to say about medicines and especially about GHI impact on upstream supply markets, even though such impact is important to understand from a pricing and supply security point of view.

In the current economic environment donors are under increasing pressure to demonstrate value for money (VFM). As a large portion of the money spent by the major GHIs goes to health technologies, an obvious question is: *are GHIs influencing market dynamics in ways that encourage VFM, and if so, how?*

GHIs do not impact pricing directly; however they may, whether by virtue of a deliberate market-shaping strategy or simply due to their funding presence, impact market structure. Changes in market structure may result in changes to pricing, supply availability and/or product characteristics. But attributing market impact resulting directly from a given GHI intervention is challenging, because of system interdependencies on two levels:

1. Interdependencies between policies and interventions by various funders (where funding is fragmented) and actors - making attribution a challenge
2. The relationship (often inverse) between interventions which attempt to impact price and those which aim to impact supply security, quality, acceptability and delivery - making it difficult to isolate the impact of a single intervention or distinguish which intervention has had the most impact

Where the GHI is the dominant funder of a product category, we can be relatively confident that the GHI's actions are a major influence on changes within that product class. Where the product funding is more fragmented, interviews with GHIs, independent experts and industry can guide our conclusions about relative influence.

The second challenge – interdependencies between interventions aimed at different aspects of access - highlights the need to take a comprehensive approach to monitoring and measuring the market impact of GHIs, as a contributor to health impact. Interventions aimed at price reduction are an obvious objective, but this must be balanced by a focus on achieving or maintaining supply security, quality, acceptability and availability.

If we map standard value for money dimensions against GHI market shaping activities, then the 'economy' category would relate to the **price** of the health technology and cost to deploy it. 'Efficiency' can be translated as 'lowest cost per effective use', highlighting the importance of delivery reliability and speed to promote **availability** and uptake and product **innovation** – where it promotes greater acceptance and therefore uptake. Looking further down the impact chain, **quality** becomes paramount as a contributor to the effectiveness goal of 'lowest cost per desired health impact'. **Supply security** affects price and the other parameters in a

[1] *An assessment of interactions between global health initiatives and country health systems.* World Health Organization Maximizing Positive Synergies Collaborative Group. Lancet, 373 (9681): 2137–2169, 20 June 2009.

dynamic way; sufficient supply relative to demand must be constantly managed to achieve efficient markets over time.

The entire equation, and the interdependencies between the five parameters, must be considered in monitoring and measuring GHI performance. The following examples from the report illustrate these points:

Examples of GHI market impact

The market for **second line TB drugs** is very small, providing little incentive for manufacturers to attain the WHO pre-qualification required to enable purchase with GHI funds. Supply security and pricing have consequently been problematic. UNITAID began working with the Global Drug Facility and other partners to increase diagnosis of multi-drug resistant (MDR) TB cases and to fund drugs to treat those cases. For the first time in a decade, new suppliers are seeking WHO pre-qualification, giving confidence that suppliers are specifically responding to the UNITAID funded signal that the donor funded market will expand.

Prices of LLINs can be influenced by factors such as order placement timing relative to production availability, and market leverage of the buyer. The major GHI purchasers have tried, with varying degrees of success, to influence these factors. However, LLIN prices are also influenced by factors which affect acceptability (e.g. colour, size, and shape), and length of net life. Some GHI-funded tenders have prioritised unit costs as an award criterion, while minimising criteria that would support increased acceptability (which would lead to increased use) and net longevity (which would enable less frequent distribution campaigns and therefore decrease overall costs per effective net life).

Within the **ARV market**, the sheer magnitude of Global Fund financing has had an overall catalytic effect leading to increased supplier entry and price-reducing competition, as evidenced by the number of WHO pre-qualified suppliers drawn into the market before PEPFAR and UNITAID were funding ARVs purchase. UNITAID is mandated to take a more deliberate market shaping role; in partnership with the Clinton Health Access Initiative, it has created new markets for second line ARVs and paediatric ARVs where it is the dominant funder, and where it is relatively easy to attribute resultant changes in prices, and creation of new products tailored for these markets, to its direct influence. PEPFAR's impact as a market shaper was delayed, due to the wait for the FDA tentative approval process to certify generic FDC quality and eligibility for funding. However, it has become a major funder of first line ARVs and has eventually contributed to volume growth and market maturation of the first line drugs.

GAVI is the dominant funder of **new vaccines** for developing countries and UNICEF is the procurement agent, so market impact of the two must be considered jointly. UNICEF sometimes splits awards amongst several manufacturers, some having higher prices than the lowest bidder. If 100% of the award volume is offered to the lowest price bidder, utilising 100% of its capacity and requiring it to scale up by a factor of 5 compared to current production level, this would not allow for batch failures or other contingencies and supply would not be secure. UNICEF refers to the 'vaccine security premium' which results when awards are split; in the most recent pentavalent tender, the security premium amounted to 6% of the total award for 2010-2012.

This study illustrates the inter-linkages between different market-shaping actors and interventions and the tensions between sometimes conflicting market impact goals.

These interdependencies need to be considered when donors seek to measure GHI impact on value-for-money in the health technology space. Price sometimes dominates these discussions, but price needs to be seen in relation to the other objectives driving health outcomes and also the importance of seeking dynamic as well as static improvements in health technology markets.

1. Introduction

1.1 Background

In the past decade, the global architecture around access to medicines for neglected diseases has changed: donor financing towards medicines has increased; the institutional architecture for interfacing with the market has changed, with the emergence of new global health initiatives; and the supply situation has changed, with the emergence of quality generic supply from India. One would consequently expect to see positive changes in the market for, and access to, global health technologies. However, our knowledge of the impact of GHIs on access to medicines, as an essential part of functioning health systems, is limited. This is evident from a recent Lancet2 publication considered to be "the most detailed compilation of published and emerging evidence so far" [on the interactions between global health initiatives and country health systems], which had little to say on medicines.

This subject is of particular interest in the current economic environment, in which donors are under increasing pressure to demonstrate value for money (VFM). As a large portion of the money spent by the major Global Health Initiatives (GHIs) is spent on health technologies, an obvious focus is on whether, and in what ways, these partnerships are influencing market dynamics in such a way as to encourage VFM.

1.2 Purpose

DFID has commissioned this study to assess available evidence on the market impact of selected Global Health Initiatives (GHIs). The purpose of the study is to determine whether, and in what way, GHIs have contributed to the development of a robust market for global health technologies, generating increased supply security, cost savings and increased innovation. The primary audiences will be global health initiatives having impact on the markets for health technologies and current/future donors to these GHIs. This study will provide an important tool to inform DFID's engagement with GHIs (including participation in boards and policy committees). It will also feed into the DFID multilateral review, and inform the performance frameworks that DFID agrees with GHIs.

1.3 Defining the Study Scope

1.1.1 Market Impact of Interest

Market impact can be defined simply as "the impact of a policy decision on market structure".[3] It is well known that market structure affects competition and competition affects the way that suppliers and demanders in an industry interact to determine price, quantity (including supply security) and innovation. Deriving from this knowledge, the scope of this study can be described as: "An analysis of the impact of major Global Health Initiatives on the way that suppliers and demanders in an industry interact to determine price, supply security and innovation".

[2] World Health Organization Maximizing Positive Synergies Collaborative Group. 'An assessment of interactions between global health initiatives and country health systems.' Vol. 373 :9681. June 2009, Pages 2137-2169

[3] http://www.reckon.co.uk/open/Glossary

1.1.2 Health Technology Category Focus

The study focuses on GHI market impact over time on ARVs, TB medicines, LLINs, and vaccines. The first three commodities were chosen because they comprise the majority of the Global Fund's expenditure within the "Health Products and Pharmaceuticals" category (which represents approximately 45% of Global Fund grant expenditure). As Global Fund spend is likely to be a good proxy for donor spend on these commodities worldwide, it is assumed these are the principal commodities of interest in terms of market impact and improving value for money. Vaccines were also included because GAVI is a major recipient of donor funding, therefore any positive changes in the vaccine market would be important to donors and to public health.

1.1.3 GHIs of interest

The scope will be limited to the impact of the principal GHIs (and partners/accompanying programmes) within the commodity categories above. These include the Global Fund, PEPFAR, Global Drug Facility, President's Malaria Initiative, GAVI, UNITAID and partners such as the Clinton Health Access Initiative (CHAI) and UNICEF.

1.1.4 Supplier Focus

The focus of the work will be limited to market impact of GHIs on supply coming from producers meeting international quality standards and exporting sufficient quantities to allow them to be integrated into the "upstream" global supply system. An analysis of GHI impact on infant industry in developing countries is beyond the scope of this work.

1.4 Methodology

The most scientifically valid method of assessing market impact, and resultant price changes, would be to conduct market-effect studies. This would involve setting up controlled trials with a control and test group, with longitudinal data collected on the change in market structure arising from an intervention, controlling for other variables. Studies of this nature have not been conducted in relation to GHIs and their market impact; nor is it suggested that they would be a cost-effective use of resources. In the absence of such market-effect studies, and given the 19 days allowed for this piece of work, the more appropriate method chosen was to examine process inputs of GHIs – i.e. interventions each GHI has implemented in an attempt to influence the market dynamics. Then, using knowledge of how markets react to such interventions, combined with interview data derived form experts and industry, conclusions are drawn about the impact of the GHI's interventions. In situations where one GHI dominates a product sector (for example UNITAID funds 90% of paediatric anti-retrovirals), we can be relatively more confident that the market change is driven by that GHI's actions. Where the GHI does not dominate a product sector, expert opinion, industry views and published analyses are relied on to generate conclusions about influence.

This study was divided into three phases – a market scoping phase, an industry validation phase and an analysis and report writing phase (further details below).

1.1.5 Phase 1 - Market Scoping

The aim of this phase was to better understand the market structure for each commodity and how it has evolved over time, including possible market influences of GHI interventions or other changes in the environment which may have affected the supply/demand of the health technologies of interest. Phase 1 entailed a literature

review and key informant interviews. Three days of research assistance time was allocated to assist with an initial trawl of publicly available information.

Phase 1 interviews included people from the organisations listed below. The goal of the interviews is to draw out existing published or grey literature/data on market structure, market impact over time, the interventions the organisation undertook over time in an effort to influence the market, and any evidence that the intervention can be linked to market impact. The end result of Phase 1 was a series of hypotheses about the impact that the GHI has had on the market, from which the Phase 2 industry informants were chosen.

Key Informants by commodity category:
ARVs: AMDS, Boston University, GFATM, IMS, UNITAID, CHAI
TB: WHO (GDF), IMS, TB Alliance, IDA, UNITAID, Medicines Sans Frontieres
LLINs: WHO, GFATM, UN Special Envoy on Malaria, Net Mapping Project, PSI
Vaccines: GAVI, UNICEF

1.1.6 Phase 2 – Industry Validation

The aim of Phase 2 was to validate and supplement findings from Phase I on issues of contention. Phase 2 interviews were limited to major suppliers of GHI funded programmes, including industry informants principally from generic companies based in emerging markets (as suppliers of vaccines, ARVs and TB drugs to GHI financed programmes) as well as western based multi-nationals (LLIN producers).
A standard questionnaire was not used during Phase 1 or Phase 2, as the areas of focus were different for each respondent interviewed. What was common across interviews was a focus on actions taken by the relevant GHP in an attempt to unblock challenges within a product sector along the parameters of price, supply security, availability, product innovation, and quality; discussion about confidence of attributing influence to the GHP's actions; and a discussion of counterfactual scenarios or benchmarks against which to compare impact.

1.1.7 Phase 3: Analysis and Report Writing

Phase 3 involved bringing together the results of the first two phases into a written report. The TORs required a draft report of approximately 20 pages providing;
- A retrospective narrative review of whether and how global health initiatives have had an impact on the global health technology market
- A framework for assessing the impact on static and dynamic access to medicines parameters of such initiatives

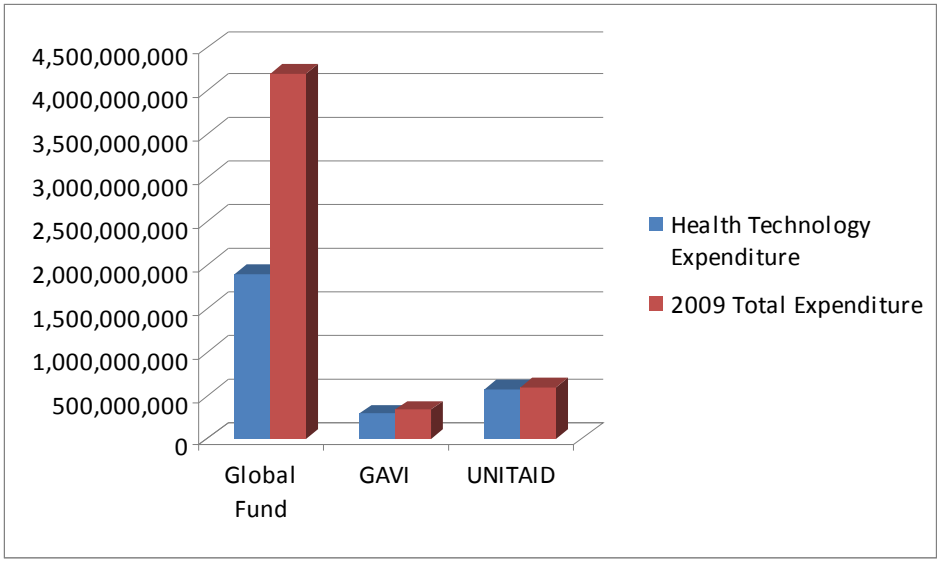
The report was peer-reviewed in its entirety and/or by commodity section as detailed in the acknowledgements section.

2. Overview and Conceptual Framework

GHIs do not impact pricing directly; rather, they impact market structure, and pricing changes may consequently result. One of the obvious impacts of the Global Fund and GAVI has been in providing substantial new finance, which has made developing country demand more credible. But the cycle through which more credible demand translates to reduced prices is an indirect and longer-term one, which can be difficult to attribute directly to a financing stream. We have evidence showing that GF and GAVI funding correlates with market entry of generic suppliers and we have empirical evidence that the number of generic entrants affects the degree of price competition and the presence of eight or more competitors is correlated with the most significant price reductions.[4] The precise way the market is shaped by a GHI depends on the underlying market characteristics of that sector and the size of demand, structure of the finance and other "process inputs" contributed by the GHI.

The portion of GHI financing directed towards commodity purchase differs, but is uniformly large. On average, over 70% of GAVI's funds are spent on vaccines, 45% of GF grants go towards medicines and other health technologies and nearly all of UNITAID's funds are spent on health commodities. Health technology expenditure for 2009 can be found in Figure 1. GAVI spent 85% of 2009 funds on vaccines (286 out of 335 million USD); assuming 45% of Global Fund grants were spent on health technologies, Global Fund spent 1.8 out of a total 2009 disbursement of 4.2 billion USD; UNITAID spent 577 million out of a 593 total 2009 disbursement on health technology purchase. Obviously even small savings on such large numbers would be interesting from a VFM point of view.

Figure 1: How Important is Expenditure on Health Technologies?



Data sources: GAVI website, 2009 UNITAID Annual Report, 2009 Global Fund Annual Report (assumed technology spend of 45%)

[4] As reviewed in "The Danger of Drug Donations (In-Kind Contributions) To the Global Fund – Adverse Market and Therapeutic Effects", Brook K. Baker, Eva Ombaka (April 28, 2008) In Press with the Lancet

In mapping GHI's activities against impact, it is obvious that appropriate market shaping activities are specific to the context and the market hurdles within a product class; however, a common framework emerges across product classes. Market shaping activities commonly target 5 areas:

1. Price (and associated costs): its determinants being industry's costs and risks, purchaser leverage, and competition (Grace, 2004[5]). GHIs can make demand more transparent and credible, and the increased economies of scale achieved by individual suppliers can, in the environment of competition or bilateral negotiations, be passed on through reduced prices. Some GHIs encourage demand pooling, in order to enhance market leverage or they may pool information, such as that on pricing, in order to achieve a similar effect. GHIs may also implement interventions intended to accelerate entry of new suppliers or decelerate exit. Although beyond the scope of this study, associated costs of implementing the technology need to be mentioned, for completeness. There are examples where GHIs prioritised higher priced products which were less expensive to implement.

2. Supply security: maintaining or attracting a sufficient level of suppliers relative to demand so as to maintain a competitive supply base and decrease risks of supply shortages.

3. Availability: delivery lead times impact on access to medicines and treatment outcomes directly. The market shaping impact of lead times is felt more indirectly; when GHIs implement interventions which keep orders rolling in on a consistent basis, this can help reduce production risks for suppliers and maintain supply security.

4. Product Innovation: improved product presentations can improve acceptability, encouraging use (efficiency) and ultimately improved health outcomes (effectiveness). GHIs can also encourage innovation towards product characteristics which increase treatment or prevention efficacy.

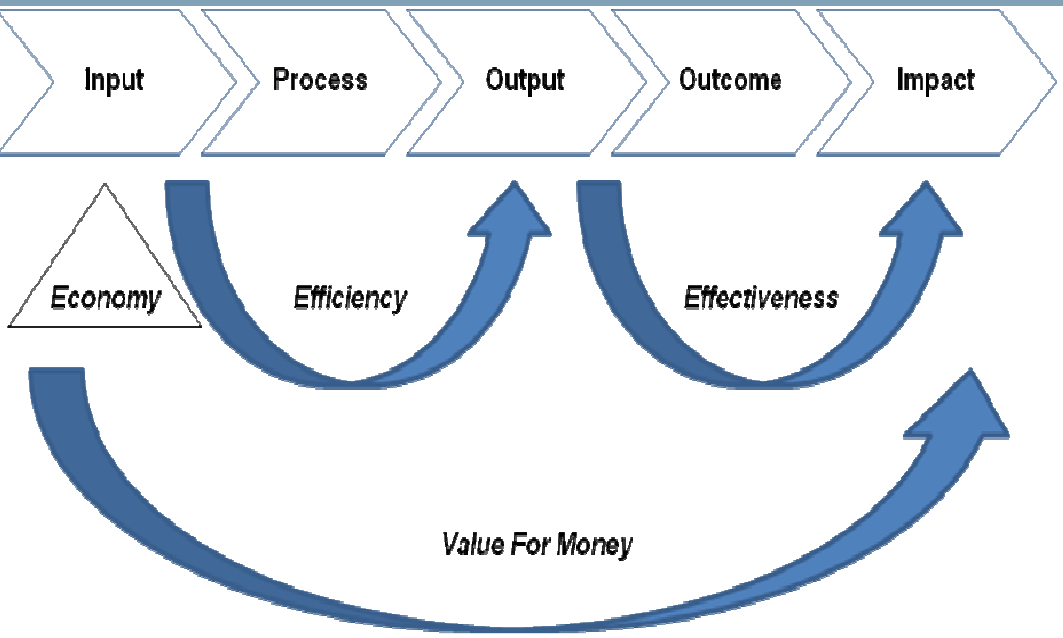
5. Quality: GHIs implement standards defining which products are eligible for purchase and indirectly, they may "raise the bar" for quality levels supplied by industry and demanded by customers outside the GHI. Quality influences whether the product is effective in its aim of disease treatment or prevention, which drives health outcomes. Perceptions of quality can also affect acceptability and consequently, product usage.

Value for Money Conceptual Framework

Figure 1 maps out a standard results chain used within the UK government to assess value for money (VFM).

[5] http://www.dfidhealthrc.org/publications/global_initiatives/GHP03paper.pdf

Figure 2: Value for Money Framework

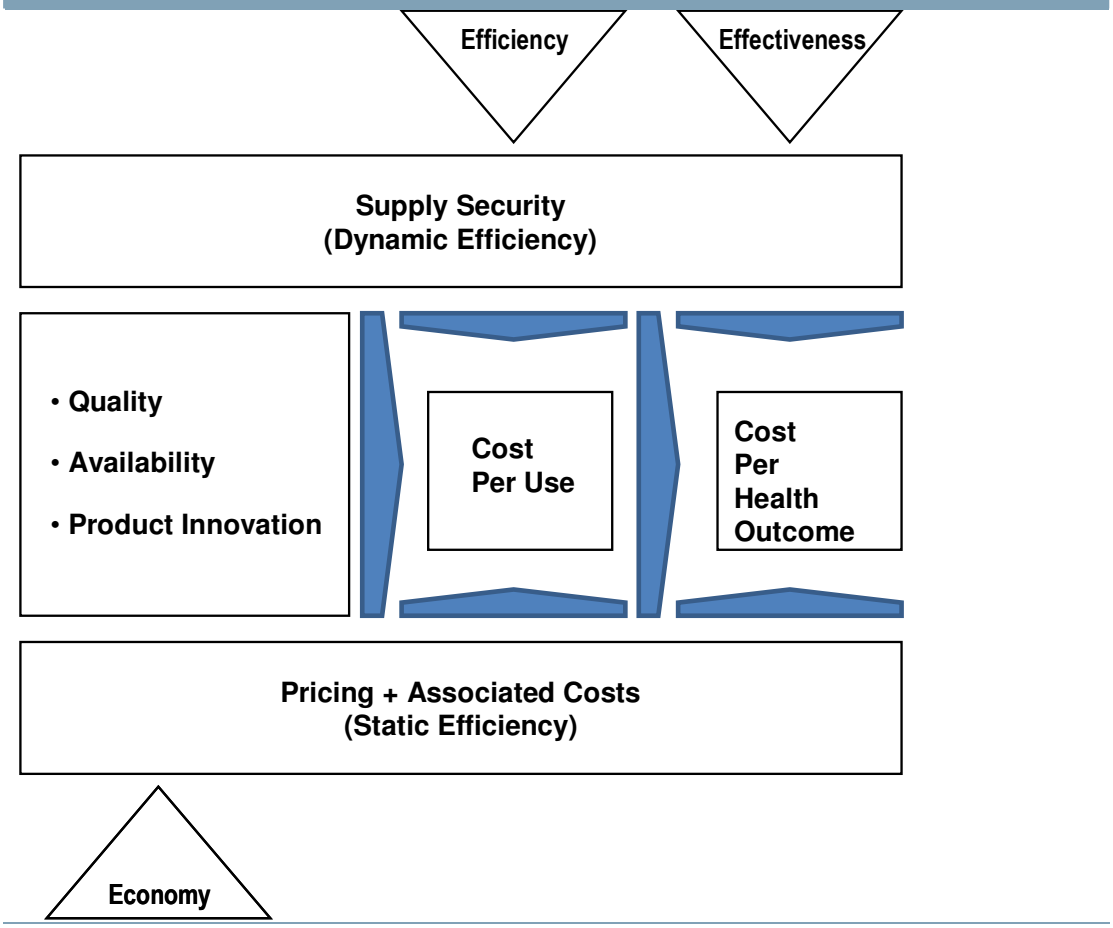


Slide source: UK Audit Commission
http://www.improvementnetwork.gov.uk/imp/core/page.do?pageId=1068398

"Economy" is the starting point – a focus on the cost of inputs. "Efficiency" looks at how well the process converts inputs into outputs, and "Effectiveness" looks at how far the outputs lead to the intended outcomes and impact. VFM combines all of these, measuring outputs, outcomes and impact compared to inputs.

If we map the standard VFM dimensions against GHI market shaping activities, then "economy" equates to the price of the health commodity (and, although beyond the scope of this study, one may also include cost of deploying the technology and GHI Secretariat commodity management or procurement costs within this section). "Efficiency" can be translated as "lowest cost per effective use", highlighting the importance of delivery speed and acceptance to ensure the technology is used. Looking further down the impact chain, "lowest cost per desired health impact" would be the equivalent of "effectiveness", where cost is the denominator and desired health impact is the numerator. Quality of the health technology, as a driver of health outcome, is paramount in this last category. Supply security affects price and overall dynamic efficiency, as sufficient supply relative to demand is required for the overall system to work efficiently.

Figure 3: Mapping VFM against GHI market shaping interventions



Interventions aimed at improvements in health technology supply security, availability, product innovation and quality increase the numerator in efficiency and effectiveness, while those aimed at reducing price decrease the denominator. The entire equation, and the balance between the 5 parameters, must be borne in mind as donors seek to develop measures of GHP performance.

The examples offered in the remainder of the report may not be an exhaustive description of all the activities every GHI undertakes to influence the market, but rather, they are meant to illustrate the framework, and especially the inter-linkages and tensions between the different market shaping goals. They illustrate the importance of considering costs in relation to the other objectives driving health outcomes and also the importance of seeking dynamic as well as static improvements in the parameters.

3. Disease Specific Findings

3.1 TB

The size of the market for TB first line drugs (FLDs) is estimated to be approximately 11.1 million patients[6]. Estimates of the publicly funded share of that range from 35% to 47%.[7] and GDF's share of the public market is approximately 49.5%[8]. The growth of GDF's market share (as a proportion of the public sector) has stagnated recently as UNDP is procuring TB drugs, itself, where it is a principal recipient of GF grants.
For MDR TB, WHO estimates that there are 432,000 cases of MDR TB; 33,000 of these cases were reported to the Green Light Committee and only 10, 598 of those reported were using Global Drug Facility second line drugs (SLDs).[9] Thus, GDF supplies approximately one-third of the overall market for SLDs.

One-third of the TB burden in the world is in India and China; 50% of first line cases are in India, China, Indonesia, Nigeria and South Africa. Seventy percent of MDR cases are in India, China, Russia, South Africa and Bangladesh.[10] The private sector plays a large treatment role in all these countries, however given the high cost of SLDs (treatment last for two years and costs between $4,000 and $10,000), the assumption is that it is only feasible for patients to access MDR TB treatment from publicly funded sources.

Within the publicly funded segment, the agencies involved in TB drug purchase are the Global Drug Facility, UNDP, direct government procurement and PEPFAR. The Global Fund finances TB medicine purchase, and procurement with its funds can be handled by GDF, countries directly (for FLDs) or UNDP (when UNDP is a GF Principal Recipient). The GF's Voluntary Pooled Purchase (VPP) Initiative[11] does not currently include TB drug procurement within its remit.

This section will focus on the market shaping activities of GDF, as the largest public procurer of TB drugs, as well as CHAI, UNITAID, and FIND. Due to different market contexts, discussion of first line TB drugs (Rifampicin, Isoniazid, Ethambutol, Pyrazinamide, and Streptomycin) is separated from that of second line TB drugs used for multi-drug resistant TB. (The second line agents listed in the WHO EDL 15th edition are amikacin, capreomycin, cycloserine, ethionamide, kanamycin, ofloxacin (or levofloxacin), para amino salicylic acid.)

Given the importance of the private sector and of the government's direct funding of TB treatment, and the consequent partial share of the market GDF procures for FLDs and SLDs, it is more difficult to attribute changes in the overall market to GDF. However, there are indicators that GDF's influence exceeds its market share and we can also observe changes in suppliers' interactions with the WHO pre-qualification

[6] WHO Global TB Control 2009 (after change in methodology for prevalence calculation)
[7] Global Alliance "Pathway to Patients" 2008 estimates 35% and the CHAI estimate, as per PHS presentation/methodology, is 47%
[8] Exact figures are unknown, since the public share is estimated; this figure represents a median, factoring in the ranges quoted in previous footnote
[9] WHO 2009 Global Tuberculosis Control Report
[10] Donald et al, New England Journal of Medicine. June 4, 2009
[11] The VPP is a voluntary, opt-in system for GF grant recipients – except in selected cases of governance or capacity problems - aiming to promote an attractive and sustainable market for the key products, as well as improve supply management outcomes through consolidated forecasts, long term supplier contracts and direct payment. The Clinton Health Access Initiative has been contracted to provide technical support for ARVs and ACTs, while Population Services International provides this for LLINs. The GF will also build countries capacities in quantification/forecasting, procurement planning, and logistics management.

process – the channel through which suppliers gain access to funding the GDF market.

Price

During the first two years of GDF, a 30% reduction in the price of first line drugs (FLDs) was achieved, due to the combined effects of aggregating demand from multiple countries via pooled procurement, standardisation of treatment regimens, and timely payment. An early evaluation of the STOP TB Partnership, (IHSD, 2003), including GDF, noted that the support costs paid to WHO were significantly outweighed by the cost savings of GDF procured drugs compared with the prices achieved by other providers or national treatment programmes, which were paying widely different prices. The evaluation concluded that this provides a strong case for promoting GDF as the preferred supplier of TB drugs procured with GF grants.

The average cost of FLDs has subsequently increased due to changes in price of raw materials, changes in exchange rates, and the increased costs (passed on through increased prices) of investments to increase quality standards to WHO pre-qualification levels. Experts warn that overly ambitious pressure on prices can lead not only to producer exit but also, for those who remain, an incentive to source less costly APIs and to use cheap packaging materials, negatively affecting quality.

Through a tender completed in February 2010, GDF has recently been able to bring down prices for FLDs by 23 % (weighted average according to 2009 procurement volumes) vis-a-vis 2007 - 2009 prices. This is the result of a more competitive approach instituted by the Procurement Agent contracted by GDF in 2009. The tender foresees bandwidths of realisable business depending on suppliers' positions as primary, secondary, tertiary supplier, as well as competitions for individual orders.

As the largest public procurer of FLDs, GDF's market shaping actions carry the most leverage and there are indications that its influence goes beyond its market share, in that the credibility which comes from being a supplier to WHO helps GDF suppliers to gain additional, private sector business. GDF also contributed to price transparency in the FLDs market overall, because it began publishing its procurement prices many years before other public funders and procurement agencies began to do so.

Second line drug (SLD) prices are high, as a result of very small markets. The first challenge is the heterogeneity of treatment regimens; resistance patterns differ country by country and patient by patient. The second challenge is the paucity of MDR TB diagnosis, further contributing to the small market size. Given that only 2% of the total amount of MDR patients worldwide are treated with GDF medicines, the implications are two-fold: a significant proportion of patients are being treated with non quality-assured drugs and GDF's market influencing leverage is obviously limited.

Despite limited market leverage, GDF achieved price reductions through bilateral negotiations with manufacturers and efforts to entice new market entrants. There have not been substantial price decreases since those initial negotiations, however there was not an expectation that there would be, given the limited supply source context where supply security has been the paramount concern and price sustainability as important factor. Most recently, GDF calculates a weighted average increase of SLD prices between 2008 and 2010 of 14%; this is attributed to increases in cost due to manufacturer quality upgrades and relevant investments.

Prices for SLDs may reduce once three or more suppliers enter each product category and it is believed this will only happen if and when the market expands

through improved diagnosis (further on this subject below). Until such time, negotiating tactics appropriate for limited supply situations are appropriate. GDF's goal is to maintain a pool of suppliers (maximum 3 per product) of quality assured products and supplies from all of them to secure sufficient quality-assured manufacturing capacities. The policy of procuring from a range of suppliers art a range of prices necessarily means that the median price will be higher than if GDF were to procure only from the lowest priced manufacturer.

In the paediatric TB market, UNITAID has worked with GDF to finance and supply nearly 670,000 paediatric treatments since 2007. Price reductions of 10-30% have been achieved on four key paediatric medicines by promoting economies of scale and stimulating competition. (UNITAID factsheet)

Supply security

The number of pre-qualified FLDs has steadily increased over time. Between 2003 and 2006, the number of pre-qualified products increased from 5 to 7 and by 2007, 12 products were pre-qualified. (McKinsey Independent Evaluation 2008) However, the increase in overall number of pre-qualified products masks the fact that for some classes, pre-qualified products are so few as to limit competition and thus GDF's leverage to benefit from price reductions.

GDF changed its procurement agent for FLDs in mid 2009 and has revisited its procurement strategy to increase emphasis on maintaining and attracting the number of suppliers in the FLD space. Tenders valid for a 2 year period are conducted, and selected suppliers enter into long term agreements with GDF in which they agree a ceiling price. The top three suppliers are offered LTAs with a certain guaranteed volume and other suppliers are offered LTAs as well, but with no guaranteed volume. From time to time, suppliers can compete for individual orders at or below the ceiling price agreed in the LTA. Any new, lower price shall forthwith become the new ceiling price. This process allows GDF to capture advantages of dynamic competition and also any possible price reductions enabled by changes in raw materials cost or exchange rates.

The number of pre-qualified SLDs is less – currently 7 out of the 11 available through GDF have either one or no product having WHO pre-qualification or SRA approval. As mentioned, the key problem is the small market size, stemming from the diversity of treatment regimens, the small number of patients and even smaller number of diagnosed patients using quality medicines. For a manufacturer, the MDR TB market is thus a relatively uninteresting commercial market, even if the supplier wins a two-year LTA to supply GDF. The exception is the fluoroquinolones; this class of medicines has other indications (respiratory and urinary tract infections, shigellosis), so supply scarcity and price is less problematic. However, 80% of SLDs have TB as their sole indication; these are the ones where API and finished product producers are very few, prices are high, and where GDF has had to actively recruit new suppliers into these markets.

CHAI is working with GDF to improve forecasts of MDR TB, gathering evidence on the distribution of the 432,000 patients worldwide and investigating their resistance patterns. UNITAID, working with FIND, GDF and the Global Laboratory Initiative, is providing funding for laboratory strengthening and to produce and roll out a new diagnostic tool which can detect MDR TB in two days (previous test took 6 weeks). The aim is to diagnose 130,000 people with MDR TB by the end of 2012. UNITAID's funding of $60 million USD will also boost the supply of MDR TB drugs and the aim is a price reduction of 20% for SLDs by 2011. (Witherspoon presentation to UNICEF Supplier Meeting 20 Oct 2008) Although, as noted, the number of pre-qualified

suppliers remains limited for SLDs, the numbers are increasing; notably Cipla has recently entered the SLD space, submitting dossiers to the WHO pre-qualification programme, and Lupin has extended their range of SLD products submitted for WHO approval. This is the first time in a decade that new suppliers are seeking WHO pre-qualification, giving confidence that suppliers are specifically responding to the UNITAID funded signal that the donor funded market will expand.

Availability

In terms of delivery lead times and reliable supply, GDF's introduction of a reliable supply of quality FLDs was attributed in its early years with catalysing the introduction and expansion of DOTS. Similarly, GDF's rapid response and emergency grant assistance have helped countries avoid interruptions in treatment programmes. (McKinsey Independent Evaluation 2008)

However, earlier evaluations noted that GDF was not meeting its lead time targets. Although GDF's lead times were shorter than alternative suppliers, only 13.6% of GDF orders had been delivered on time as of June 2003. (Independent External Evaluation of the Global Stop TB Partnership, IHSD, December 2003). These challenges persist - in April 2009, the GLC reported an average delay of 54 weeks between GLC approval and the arrival of the medicines in the country – resulting from the interplay of producer constraints and recipient country constraints.

In response, UNITAID has begun to fund the development of a Strategic Rotating Stockpile of SLD TB medicines, which has been especially useful for medicines where supply shortages and local in/country drug management issues have been challenges. The strategic stockpile enables the placement or orders in advance of orders from countries, and in line with forecasted demand. The effect of placing the order in advance of country orders has been to maintain the interest (and market presence) of producers of niche TB drugs, enable sustainable pricing terms due to enabling better production planning, and lend credibility to GDF forecasts for the forthcoming scale up in demand of SLDs.

UNITAID is also finalizing a "Strategic Rotating Fund" in partnership with GDF, with the intention to shorten country access to SLDs for eligible countries.

Product Innovation

Early on, GDF catalysed the uptake of compliance-enhancing packaging and fixed dose formulations, thereby promoting alignment with WHO guidelines, improved treatment outcomes and better drug supply management.

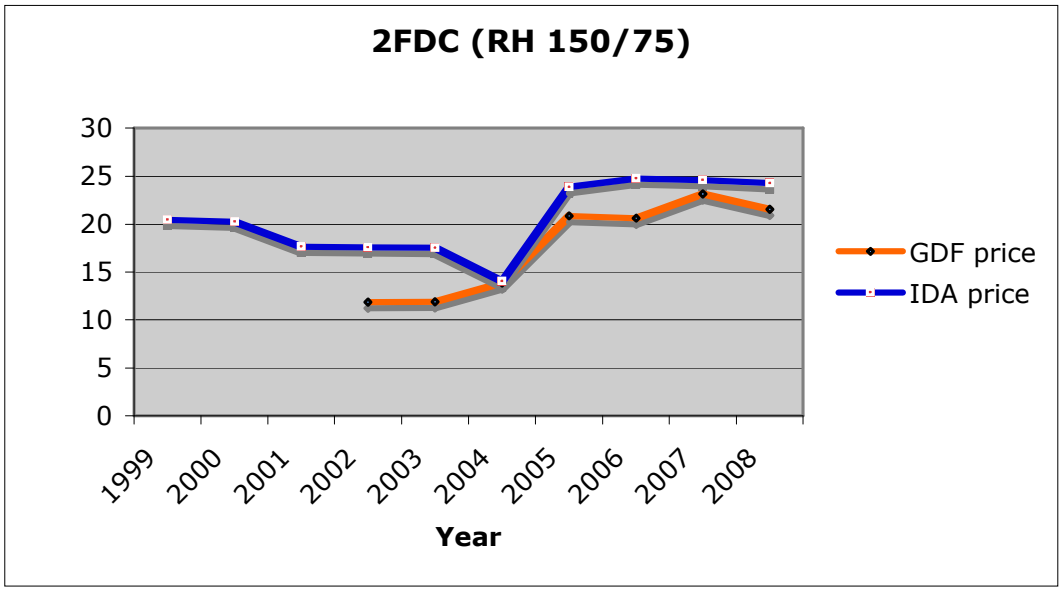
More recently, UNITAID has been stimulating market interest in paediatric TB medicines by pro-actively engaging manufacturers to develop child-friendly FDC formulations. UNITAID is providing funding for coverage of 750,000 patients between 2007 and 2011 and has been credited with the emergence of new and better products including dispersible and blister formulations, products with an improved shelf-life and products with WHO Pre-qualification (PQ). In 2009, WHO changed their recommendations for the dosages of paediatric TB medicines. In order to motivate producers to develop new appropriate-strength formulations for children by the end of 2011, UNITAID continues to fund scale-up and is working on reliable forecasting to ensure availability of current formulations throughout transition period to new formulations. UNITAID has catalysed uptake of the paediatric medicines and implementation of proper guidelines on treatment of children.

Quality

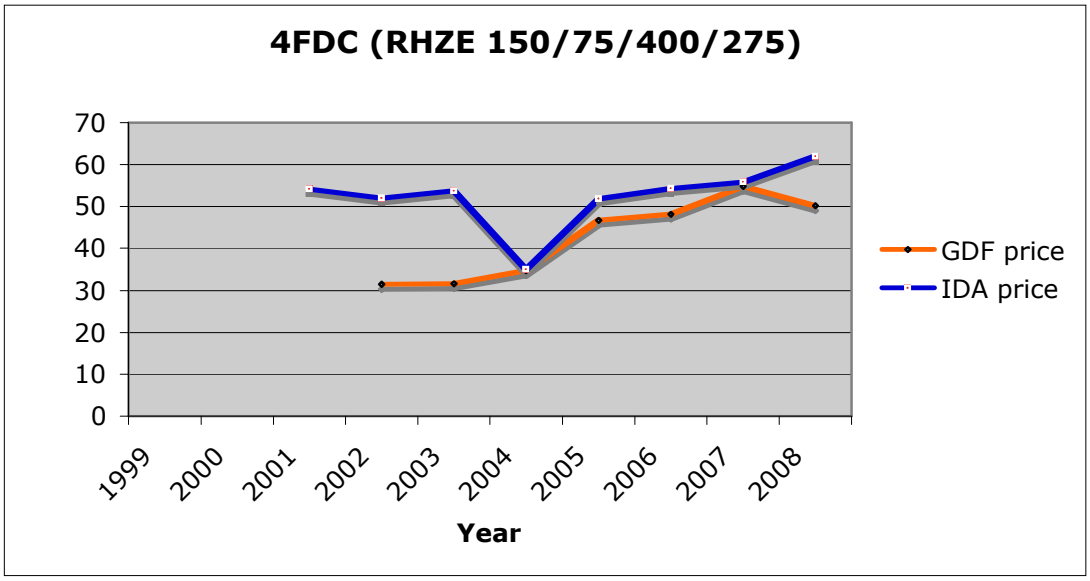
GDF's quality requirements have been credited with producing externalities - countries demand higher drug quality and suppliers offer higher quality - even outside GDF transactions; for example Kenya and Uganda now require that TB drugs bought via national tender match those supplied by GDF. (McKinsey Independent Evaluation 2008). GDF also links drug deliveries with in-country monitoring missions and technical assistance aimed at promoting good drug management practices in the country, so the quality of the overall TB health system is improved in line with the quality of drugs.

GDF has traditionally taken a tiered and pragmatic approach to quality standards, aligning their standards with the market circumstances. In 2003, QA policies were tightened and FLD suppliers were asked to submit their pre-qualification dossiers to the WHO Pre-qualification project (PQP). By 2004, four producers had become qualified. The direct costs of this decision can be seen in Graphs 1 and 2 below, which show the evolution of selected formulation prices between 1999 and 2008 and the incremental cost of quality assurance. (Graph Source: J. Caudron, TB Medicines Market 1999-2009, Submission to the UNITAID Expert Working Group on Market Impact. Figures are taken from the MSH International Drug Price Indicator Guide and compare GDF and IDA prices.)

Graph 1: Direct cost of quality assurance for TB FLD



Graph 2: Direct cost of quality assurance for TB FLD



GDF is again in the process of tightening its quality policies[12], aligning with those of the Global Fund. GDF's current policy has been to require WHO pre-qualification or marketing authorisation by a Stringent Regulatory Authority (SRA). However, if an insufficient number of suppliers meet those requirements, then quality risk assessments are conducted by an expert review panel (ERP) to assess whether a product can be eligible for procurement during a limited period of time. To be eligible for ERP review, the supplier must have an application accepted for assessment at the WHO PQ programme or at an SRA and must also be manufactured on a site certified as GMP-compliant (Good Manufacturing Practice). The ERP system is seen as an effective way to bridge towards higher quality standards whilst in the interim maintaining supply security and the incentive for investment in pre-qualification. The difference between Global Fund and GDF's standards (and the issue that will be aligned) stems from the cut off point/definition of "insufficient suppliers" which allows the ERP mechanism to kick in. The ERP process is also seen to have externalities, as others procuring TB medicines can rely on the results since the outcome is publicly available.

Discussion/future challenges

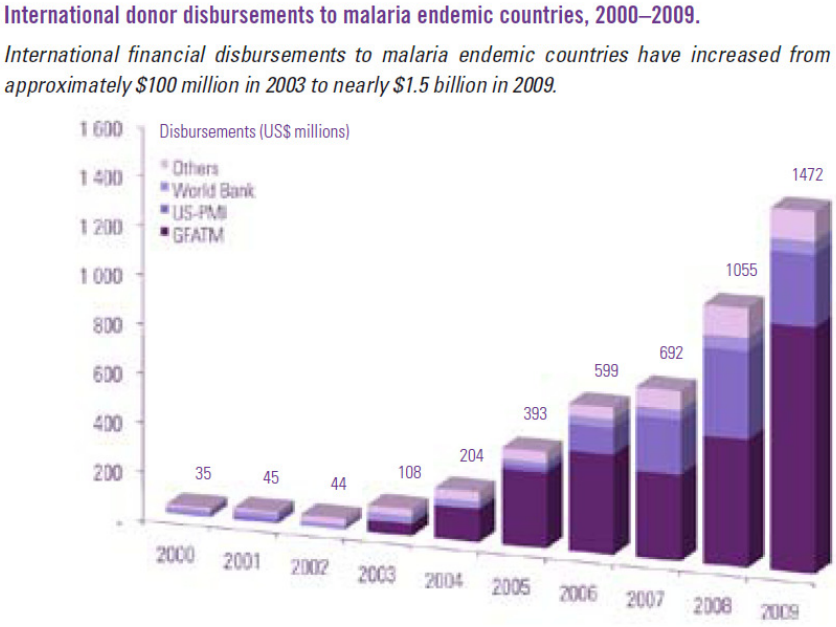
The characteristics and challenges of the FLD and SLD markets are very different and require different strategies and plans. While the role of the current market shapers addressing TB burden in low resource settings is laudable, impact would be greater if GDF's share of the public market were greater and if GDF's influence over the private sector were greater, thereby reducing the share of substandard quality products. If such a large portion of the TB burden is in countries which are not aid-dependent and where the private sector plays a large role, TB control and treatment strategies surely must emphasise these countries and private channels of care. It is perhaps the externalities and indirect effects of the GHIs, across borders and across sectors, which have more potential for impact, although these indirect effects are that much more difficult to attribute and measure.

[12] The new GDF Quality Assurance Policy was finalized in July 2010 and can be found on the GDF website.

3.2 LLINs

During the past decade, several resolutions have enabled increased recognition of malaria as a major public health problem.[13] As early as 1998, the Roll Back Malaria initiative was launched to advocate for and coordinate malaria control efforts, aiming at halving the malaria burden by 2010. Subsequently, the UN Secretary-General called for 100% coverage of malaria control interventions by 2010.[14] Insecticide Treated Nets are a key malaria intervention, which exert a community 'mass effect'[15] together with personal protection of the person under the net. Major increases in donor funding [Graph 3] have enabled a massive scale up of ITN distribution, aiming to provide universal access to an LLIN.

Graph 3: Growth in malaria funding



Slide source: page 29, Roll Back Malaria Progress and Impact Series, March 2010

[13] - WHO, Resolution AFR/RC50/R6, Roll Back Malaria in the African Region: a framework for implementation. In: Fiftieth session of the WHO Regional Committee for Africa, Ouagadougou, Burkina Faso, 28 August-2 September 2000, Final report. Brazzaville, World Health Organization, Regional Office for Africa, 2000, (AFR/RC50/17), pp. 19-22; WHO, Resolution AFR/RC53/R6, Scaling up interventions against HIV/AIDS, tuberculosis and malaria in the African Region, In: Fifty-third session of the WHO Regional Committee for Africa, Johannesburg, South Africa, 1-5 September 2003, Final report. Brazzaville, World Health Organization, Regional Office for Africa, 2003 (AFR/RC53/18), pp. 20-22; Resolution WHA58.2, Malaria control, Geneva, World Health Organization, 2003 (WHA58/2005).

[14] On World Malaria Day in April 2008, UN Secretary-General Ban Ki-moon called for universal coverage with proven malaria tools by the end of 2010, and appointed Ray Chambers as the UN Special Envoy for Malaria to mobilize global support for action on the disease.

[15] Curtis C, Maxwell C, Lemnge M, Kilama WL, Steketee RW, Hawley WA, Bergevin Y, Campbell CC, Sachs J, Teklehaimanot A et al: Scaling-up coverage with insecticide-treated nets against malaria in Africa: who should pay? Lancet Infect Dis 2003, 3(5):304-307.

Due to differences in the operational definition(s) of universal access[16], as presented in one published paper[17], one advocacy report[18], and on the RBM website[19], a range of estimates have been given for the number of nets needed to achieve universal coverage over the 3 year scale up period of 2007-2010. Using the the Global Malaria Action Plan (GMAP) figures, it is estimated that 730 million LLINs would need to be distributed in order to protect populations at risk during 2007-2010. According to GMAP, the 50 to 100 million nets already distributed (mostly in sub-Saharan Africa) would remain effective for the two years after the GMAP was produced. Approximately 315 to 340 million new LLINs would be needed annually in 2009 and 2010. For Africa alone, 250 – 300 new LLINs would be needed to reach universal coverage by 2010.

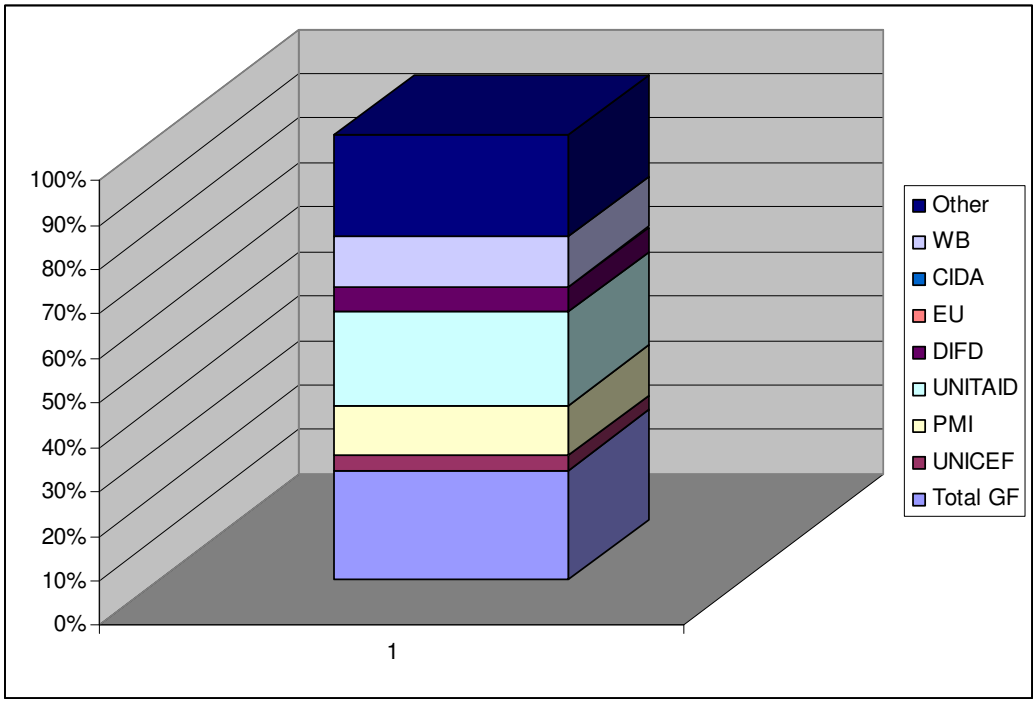
According to the Alliance for Malaria Prevention, the remaining need as of mid 2010 to meet universal coverage was 250 million nets. As of July 2010, approximately 225 million nets had been financed or pledged, leaving an overall gap of 25 million nets. (source UN Envoy's office). It should be noted that market size estimates are predicated on the assumption that net life is three years. However there is emerging evidence that net life is variable, calling some to push for operational research into net longevity and use and an increased emphasis on routine distribution systems including the private sector, to supplement mass campaigns.20

Under the three year life span assumption, the LLIN market post 2010 will become a replacement market, fuelled by 2008 nets which will be 3 years old and need to be replaced. Current orders, this "bubble/catch up year" are believed to be taking up the current total capacity of LLIN manufacturers combined, thus a key concern for the malaria community of late has been co-ordinating the requirements arising from the new funding with available production capacities.

Funding for nets comes primarily from the Global Fund, the US President's Malaria Initiative (PMI), UNITAID, bilateral donors and the World Bank. Graph 4 below provides funding market share data for 2009, as reported by manufacturers to the net mapping project. These figures should be taken as indicative only, as manufacturers are not always aware of the ultimate funder. The Global Fund's share is likely understated, as we know that the Global Fund became the largest single financier of nets with the procurement of 121 million nets approved for Phase 1 of Round 8.

[16] Based upon differing assumptions of target groups and different assumptions about delivery channels
[17] Miller JM, Korenromp EL, Nahlen BL, R WS: Estimating the number of insecticide-treated nets required by African households to reach continent-wide malaria coverage targets. Jama 2007, 297(20):2241-2250.
[18] McKinsey: We can't afford to wait: the business case for rapid scale-up of malaria control in Africa. In.: Malaria No More on behalf of the Roll Back Malaria Partnership; 2008.
[19] http://www.rbm.who.int/psm/index.html
[20] Jo Lines, WHO, personal communication

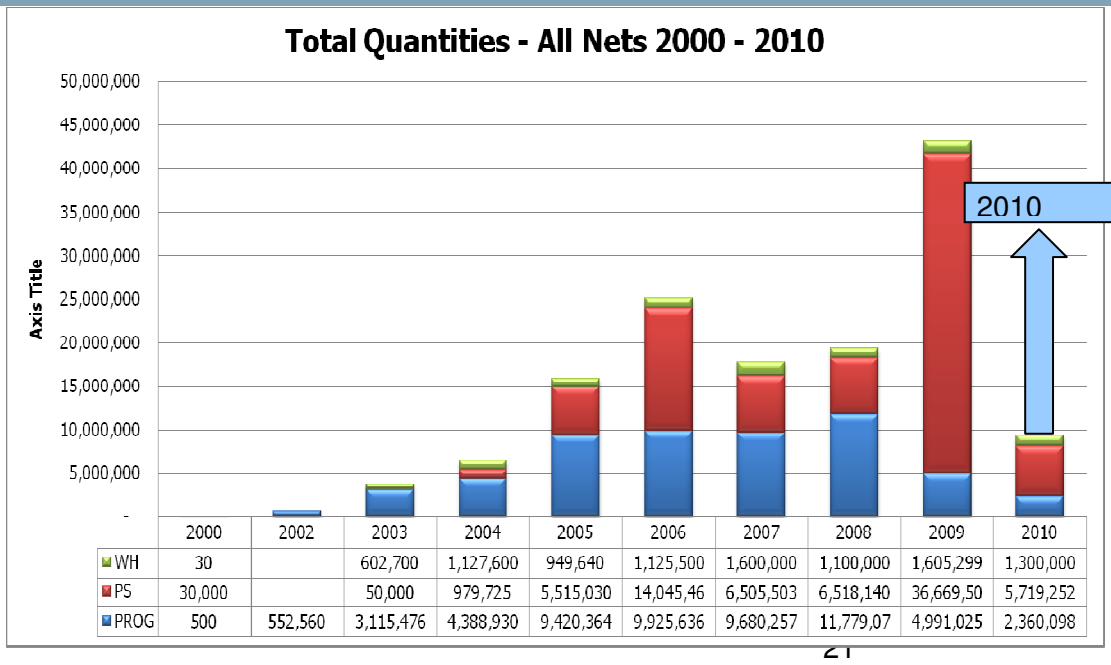
Graph 4: 2009 Funders of LLINs (indicative)



(Data for slide provided by USAID's Net Mapping Project)

Procurement of nets is handled by UNICEF (on behalf of UNITAID or countries, using aid or domestic funds), Population Services International (PSI) (on behalf of countries participating in the GF VPP) and John Snow International (JSI) (on behalf of PMI). UNICEF reports that it procured 42 million nets in 2009, which would have been half of the annual global procurement as reported in the USAID Net Mapping project, giving UNICEF substantial market leverage. Some of UNICEF's volume has shifted to PSI over the past year when GF contracted PSI as the agent handling VPP orders. Fifty five million LLINs have been processed through the VPP since its inception.

Graph 5: UNICEF's procurement volumes 2000 – 2010



	2000	2002	2003	2004	2005	2006	2007	2008	2009	2010
WH	30		602,700	1,127,600	949,640	1,125,500	1,600,000	1,100,000	1,605,299	1,300,000
PS	30,000		50,000	979,725	5,515,030	14,045,46	6,505,503	6,518,140	36,669,50	5,719,252
PROG	500	552,560	3,115,476	4,388,930	9,420,364	9,925,636	9,680,257	11,779,07	4,991,025	2,360,098

(Data source: UNICEF)

Supply security

In recent years, the LLIN market became less concentrated; in 2004 there were only two WHOPES recommended suppliers while in 2009 there were seven. Experts opine that the two dominant suppliers which had 80% market share only 2 years ago now have about 65% market share.

Given the proximity of supply capacity to demand forecasts during 2009 and 2010, UNICEF structured its procurement differently from 2009, awarding fixed quantities to a variety of suppliers in order to stimulate competition and secure commitments.

It has been opined that a PSI requirement of a performance bond of 10% of the tender value has the opposite, anti-competitive effect; larger firms will be more capable than smaller ones to part with such working capital, therefore smaller firms will be precluded from participation in larger tenders. PSI asserts that such a performance bond is standard practice. UNICEF's LTA contracts provide similar assurances, but without the need for the producer to front capital.

The year 2010 was expected to be the "bubble year" when the largest capacity will be required to meet universal coverage. However, there have been delays in the availability of funding, and funding has arrived unpredictably, which creates pressures on demand and results in higher prices.

Availability

The Global Fund foresaw challenges in meeting universal coverage goals, given frequent delays experienced due to country capacity for forecasting, developing procurement plans and delays in grant signing and fund disbursement. Problems such as unclear LLIN specifications not directly related to net efficacy, and community acceptance and utilisation have contributed to lengthy tender processes of GF grantees. It was envisaged that the VPP mechanism would help overcome these bottlenecks; as stated in a Global Fund Information note available online: "The

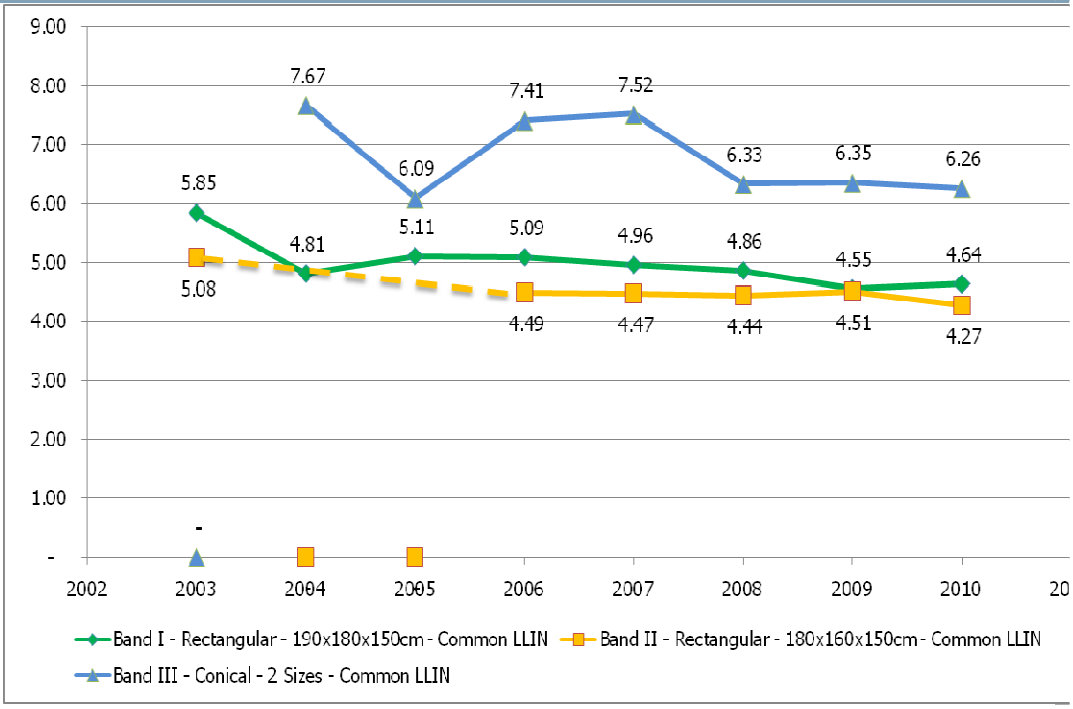
main objective of VPP is to provide support to countries to facilitate timely procurement of medicines and health products during grant implementation, and improve access to these critical health products for their populations".

The VPP mechanism has been credited with enabling an innovative "mini-grant" to be signed for Nigeria resulting in net distribution in late 2009. And, by overcoming other challenges, VPP has accelerated net procurement in a number of other countries such as Indonesia and Uganda as well. The LLIN average response time of Procurement Agents (from submission of PR requirement to receiving a proforma invoice from procurement agents) is 53 days (25-86 days). The turnaround time of PRs (submission of proforma invoice by procurement agents to confirmation of order by PRs) is 69 days. These figures represent an improvement relative to average procurement process lead times at country level, being 180 days. (Global Fund report on VPP, submitted to the second MDC meeting)

Price

According to several in-depth, programme level costing studies in sub-Saharan Africa, the cost of LLINs is the largest cost driver of net distribution programmes, making LLINs an important focus of value for money efforts. Global Fund grant recipients paid a median price of $5.7 per net in 2004, declining to $5.3 in 2009. (Global Fund 2010: Innovation and Impact Report) UNICEF prices for the most commonly procured nets have dropped below the $5 mark already in 2007. Graph 6 below provides the weighted average of UNICEF prices for LLINs over time. There has been a steady but slow decrease in the prices, which might have been expected in an environment of volume increases arising from universal coverage targets and increased competition. There is also a gradual closing of the price variations between the different types of LLINs.

Graph 6: LLIN weighted average prices



Slide source: UNICEF. Prices are FCA various locations, showing the difference in price for different LLIN sizes

In the Global Fund's 2010 performance indicators, there is the goal to improve LLIN prices by 5% against the benchmark price of $5.3. The goal of a 5% price reduction would bring price per net to just above $5 per net. Since LLIN prices are influenced by factors such as order placement timing relative to production availability, product heterogeneity in terms of tailored specifications, and market leverage (affected by volume, procurement method and management), it is difficult to say whether this target is achievable for GF for the reasons further elaborated below.

The procurement of 121 million LLINs was approved for Phase 1 of Round 8. If these nets were procured at an average price of $5 instead of $5.30, the aggregate savings on that round of financing would be $36 million USD.

For reference, the Global Fund Board decision to establish VPP states that the 2007 budgetary implication would be $1.13 million USD, enabling the creation of 5 positions:**http://www.theglobalfund.org/documents/board/15/GF-BM15-CP15 Decision.pdf**

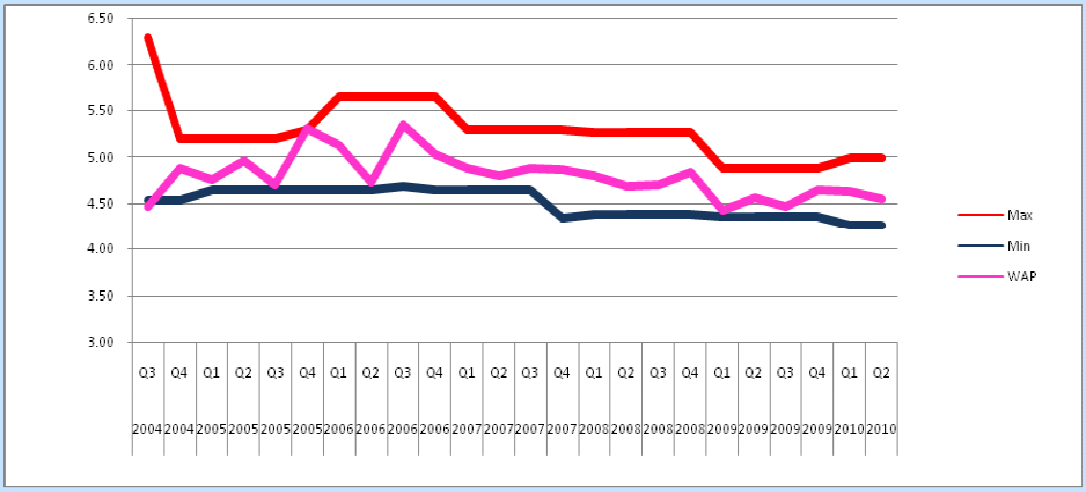
To fully compare the costs, one would need to include the Secretariat costs for years subsequent to of 2007 as well as the fees of consultants and agents also involved in VPP.

As of January 2010, 55 million nets have been processed through VPP, so assuming 5% savings on these nets only, the result would be a $16.5 million USD savings.

UNICEF uses pooled procurement and target bound contracts to ensure some stability in the market served by the organization. Evidence of the effect of timely procurement planning aligned with the timely availability of funds was demonstrated in 2009 through the experience with UNITAID funding to UNICEF. Using the example of white coloured nets of the following dimension: 190x180x150, one can see that the Weighted Average Price paid under UNITAID procurement was consistently close to the minimum price. See Box 1 below describing procurement in 2009, Q1, Q2, Q3, when most of the procurement was for UNITAID programmes.

Box 1: Case study - How alignment of secure funding and advance order planning enables reduced prices and market stabilisation

Variation per quarter in Actual Price Paid by UNICEF
Quarter 3 2004 to Quarter 2 2010



Given the fact that procurement decisions are based on price *and* ability to deliver within the given timeframe, the following observations can be made:

- Despite the fact that there were severe limitations on production capacities between 2004 and 2008, there has been a steady decrease in maximum prices. The slight increases in maximum prices correpond with introduction of new WHOPES recommended products and new suppliers, easing the pressure on production capacities.
- Minimum prices follow similar trends as maximum prices, are less erratic and decreases are less significant.
- An important observation is the decrease in the gap between the maximum and minimum prices as a result of the increase in market competition. This partly contributes towards the decrease of Weighted Avarage Price (WAP).

The WAP variations reflect the influence of funding availability and advance planning on price. The 2009 experience shows the achievement of lower WAP as a result of good planning as most of the procurement was done for UNITAID supported countries, where funding was available, allowing for advance production planning and volume committments. Conversely, when funding is erratic and will soon expire (e.g. if it is linked to GF milesones) then purchasers are in a weaker negotiating position, orders not predictable and prices paid are usually higher.

UNICEF's method of procurement involves annual tenders, based on annual forecasts from countries and partners that procure through UNICEF. UNICEF then pools all the requirements into one request for proposals, and bidders are asked to submit offers on all their standard sizes and colours. UNICEF then extracts that information to obtain comparable bids. Selected manufacturers are offered Long Terms Agreements (LTAs) for period of one year against which Purchase Orders can be placed for the duration of the Long Term Agreements under the terms and conditions provided with LTAs. UNICEF's market leverage is exerted during the LTA tender period, as this is when manufacturers see the aggregated annual volume available through UNICEF, and offer their best terms of conditions to try and achieve selection. Then dynamic competition is exerted each time a country submits funds for a specific order, at which point UNICEF selects the supplier, based on availability and delivery speed.[21] In 2009, due to the anticipated tight alignment between supply and demand in the context of the universal coverage scale up, UNICEF introduced a major shift in LLIN procurement strategy. UNICEF provided projections of quantities to be purchased and allocated volume in advance to suppliers, in order to ensure that orders would be filled.

In comparison, GF grant recipients had traditionally procured their own nets (though some went through UNICEF and other procurement agents) and the GF observed large price variations in prices paid by its grant recipients, stemming from several challenges. First, the Global Fund accepts country's LLIN preferences with regard to specifications so long as the specifications do not limit competition. (Increased customisation can lead to a narrower competitive field, increased prices and increased production lead times.) When countries tailor specifications so as to narrow the competitive field (e.g. the requirement for biodegradable bags which can only be met one manufacturer) it creates a perception of allegiance to that supplier and governance problems, and the funder has a value for money challenge of how to ensure that the county specifications are justified. There has also been a view that better price reductions could be achieved through combining the collective demand of GF grant recipients.

Due to these challenges, LLINs became a priority commodity of the VPP. The same Global Fund information note referenced previously, states "The pooled procurement mechanism is therefore designed to aggregate order volumes to leverage the Global Fund purchasing power, in order to obtain best pricing and delivery outcomes from suppliers of critical healthcare commodities. In addition, VPP is expected to promote an attractive and sustainable market for key products." Considering 85% of the total order value of VPP has been spent on LLIN procurement, evaluating VPP at present is largely an evaluation of performance with LLIN procurement. The Office of the Inspector General (OIG) is currently conducting a review of the VPP and results are expected by end of October.

However, making cost comparisons across time and between funders/procurement agents is complicated by non-comparability of data. Many Principal Recipients (PRs) quote LLIN prices paid in CIP/CIF terms and so that is what is reported in the PQR system. GF is encouraging countries to report consistently in FOB terms, but until this is consistently done, the different delivery terms can easily add 10-15% to the cost of a bednet, making data non-comparable. For example, for LLINs of size 160 x

[21] UNICEF may also be supplied at the reduced price, if the market price has dropped since the LTAs were negotiated. Suppliers having LTAs with UNICEF are required to supply UNICEF at their lowest price offered to any buyer, due to UNICEF having "most favoured nation" status.

180 x 150 cm the PQR[22] show a substantial difference in the prices quoted across incoterms:

Terms	Transactions	Avg Unit Cost	
CIP	14	$	5.13
FOB	23	$	4.55

As noted previously (UNICEF data, Graph 6), there are also significant price differences across the size of bednets. The following comparison shows the differences in the GF FOB unit cost for two common rectangular LLINs[23]:

Size	Transactions	Unit Cost (FOB)	Qty
190 x 180 x 150 cm	12	$ 4.99	3,257,127
160 x 180 x 150 cm	23	$ 4.55	6,166,497

GF FOB prices are slightly higher than UNICEF's prices for the same size nets. In summary, price comparisons should be done at the level of net type and accounting for delivery terms (CIF versus FOB/FCA).

There have been stakeholder concerns about GF's ability to achieve VFM principally related to two issues:

- The collective buying power of countries has not been fully leveraged in the way tenders have been managed, since VPP LLIN tenders have been a series of sequential orders, rather than pooled together. This has been compared to UNICEF's methods which involve a forecast for standard 3 or 4 specifications, negotiating with producers en masse when the annual tender for LTAs is issued, thereby leveraging collective buying power, and pre-booking volumes from a range of suppliers.
- In the Nigeria nets procurement of 26.9 million nets, the price achieved by VPP's procurement agent was US $11 million dollars above the grant budget. After negotiation, the overall price was reduced by US $12 million, making the price per net US $5.05. However concerns remained about the potential for price reductions, given that VPP is voluntary, orders are ad hoc and the GF is reluctant to infringe on countries rights to tailor design specification and timing of orders.

There are alternative models that both aggregate demand and allow some flexibility for countries, for example the Access RH model, whereby UNFPA aggregates country demand for oral contraceptives (OCs) and negotiates framework contracts with suppliers with minimum volume guarantees. Countries in the scheme then access the framework contract terms, either through their own procurement process or using UNFPA as an agent. The model works because the World Bank has signed an MoU with participating countries, and this enables the countries to access to loans for oral contraceptive order placement, which are repaid once donor funds are received. As with the example of UNITAID funding LLIN procurement under UNICEF, the key is the advance planning enabled by simultaneous matching of demand, supply and finance.

[22] Data source: Patrick Aylward, Global Fund VPP
[23] Data source: Patrick Aylward, Global Fund VPP

Quality

In LLINs, the WHO Pesticides Evaluation Scheme (WHOPES) system operates similarly to the WHO Pre-qualification, in that it provides a minimum standard for eligibility of purchase with public funds. A supplier is eligible for purchase with public funds whether having WHOPES interim or WHOPES full approval. Interim approval confirms that the product has been washed 20 times and therefore it is expected to last 3 years. Full approval means that the product has been tested in the field and verified. However, one important difference between LLINs and pharmaceuticals is pre-qualified drugs of the same generic are exactly equal, whereas not all nets meeting the minimum WHOPES criteria are equal. The implications of this are discussed further in the Innovation section.

The Global Fund requires grant recipients to conduct quality assurance testing upon receipt of the nets. WHO has published a guideline offering how to assess quality but there is no global norm for how to conduct such testing; UNICEF, Crown Agents, PSI etc all do it differently. UNICEF introduced rigorous inspections and laboratory testing in 2005 and claims to have witnessed a significant improvement of the quality of LLINs supplied as a result.

It has been suggested that the WHO ITN specification guidance document could be improved, for example, explaining what should be done with nets in “marginal pass” situations, considering whether the QA is practical (cost-effective and quick) to conduct, considering whether weight should be checked.

Product Innovation

The price of the LLIN needs to be seen within a more comprehensive framework of cost-efficiency - cost per year of effective net life in this case. Instead, some tenders have prioritised unit costs as an award criterion, while minimising criteria that would support increased acceptability - leading to increased use - and net longevity – enabling less frequent distribution campaigns and therefore overall decrease in costs per effective net life. There is a view that the WHOPES criteria essentially flattens the market, by serving as a lowest common denominator and not recognising product differentiation characteristics which might result in a greater overall cost effectiveness. By relying on WHOPES as the criteria for pre-qualification, and prioritising unit cost in tender criteria in GHI-funded tenders, incentives to invest in any product features exceeding the WHOPES criteria are reduced. For instance, there is no incentive to develop a 7 year net which would cost more but last longer. The technical scope to increase net insecticide life is great but the procurement system would need to provide an incentive for manufacturers to make that investment. WHO has begun research to look into differences in net durability and insect resistance and it is expected that more attention will be given to these issues.

Discussion/Future Challenges

A first challenge is constructing GHI interventions to lower prices when very little is known about cost of goods and how these differ according to differences in product characteristics, and also bearing in mind the need to create incentives for innovation and allow local preference to be expressed in tenders. WHO has proposed operational research to study net acceptability and use in communities and assess differences in net performance at country level. (Jo Lines, WHO, personal communication)

A second issue is distribution and effective use. Communication between stakeholders has been challenging – between donors, procurement agents and even within countries. This affects forecasting and intelligence about how many nets are already in circulation and where they have been sent. Similarly, nets can be

distributed but not used. Studies have shown that there is high and equitable net coverage immediately after a campaign but coverage two years later is disappointing. (Jayne Webster, LSHTM) Consequently, experts opine that countries should give more emphasis to routine channels of input, such as EPI and antenatal visits, as well as through the private sector.

Funding has massively increased in pursuit of universal coverage, however the degree of attention to market shaping has been less than ideal. As noted, the impact of the VPP's LLIN market shaping was positive in terms of accelerating procurement (availability), but there are not yet indications of market impact in other respects. More positively, UNITAID committed US $109 to UNICEF to purchase and distribute 20 million LLINs to eight African countries over 2009-2010, and this helped maintain supply security and price stability through order predictability and forward commitments made by UNICEF. The net mapping project has also been a useful intelligence gathering and communication exercise.

3.3 ARVs

Thirty three million people are living with HIV/AIDS, 97% of whom are in developing countries. Approximately 5.2 million patients are on treatment in low and middle income countries and experts believe that approximately 1 million patients in upper-income countries are on therapy. The GF provides ARVs for about 2.5 million people and PEPFAR is the other major financier of first line ARVs. UNITAID provides limited first line ARV financing and is the dominant financier of second line and paediatric ARVs (70% and 90% of the market respectively is financed by UNITAID).

Price

It is well known that the entry of generic suppliers into the ARV market was responsible for bringing the annual price of triple combination therapy down from $10,000 to $350 in a single year.[24] And an econometric study by Luccini and colleagues, analysing ARV procurement prices in Brazil plus 13 African countries, and observing 1030 transactions, provided the first empirical evidence that increased competition, more than originator's philanthropic differential pricing offers through the Accelerated Access Initiative, had provided the driving force for ARV price decreases.[25] Wirtz et al 2009 (BMC Public Health) analysed global purchases of 12 ARVs as reported in the Global Price mechanism from the WHO and found three factors influencing country's ARV prices: whether the product is generic, the socioeconomic status of the country and whether the country is a member of the Clinton Health Access Initiative consortium. Factors which did not influence procurement were HIV prevalence, procurement volume, and whether the country was a PEPFAR focus country. Similarly, Waning et al 2009 (WHO Bulletin) showed empirically that ARV purchase volume at individual country level is not correlated with price but membership in the CHAI consortium is correlated with paying lower prices.

CHAI's work in this product sector has been instrumental. Since 2003, CHAI has led price negotiations with major generic ARV manufacturers on behalf of its procurement consortium, which includes 74 countries. Major price reductions have been achieved in negotiations, for example the price of D4T+3TC+NVP was agreed

[24] Oxfam briefing paper no 26. Generic competition, price and access to medicines? The case of ARVs in Uganda July 10, 2002

[25] Luccini et al. "Decrease in Prices of Antiretroviral Drugs for Developing Countries: from political "Philanthropy" to Regulated Markets" In: Economics of AIDS and access to HIV / AIDS care in developing countries. Issues and challenges. 2003 Jul:169-211.

at $132 in 2003, whereas the lowest price on the market for that combination had been $281.

CHAI also engages in targeted market shaping activities to unblock bottlenecks. CHAI facilitates market entry of quality assured manufacturers and helps suppliers implement more cost efficient manufacturing practices and source low cost raw materials. On the demand side, CHAI develops robust demand forecasts that reduce risks for suppliers and help them optimise production planning. Although CHAI does not act as a procurement agent, aggregating demand and making purchases on behalf of countries[26], the *economic* effect of the CHAI consortium operates similarly. The CHAI framework agreement makes aggregated demand of participating countries more transparent and suppliers commit to reduced prices in exchange for a portion of that volume. It should be noted that CHAI's work, though instrumental, would not have been possible without the financial muscle of GF and UNITAID, which provided country finance for ARV purchase. So the synergistic effect of GF and UNITAID finance, along with CHAI's targeted market shaping activities, is responsible for price reduction in the ARV sector.

Quantifying savings attributable to CHAI

CHAI worked with the South African government on the strategy and execution of its most recent tender. Compared with prices South Africa negotiated under its previous tender without CHAI's support, savings of $250-300 million per year can be expected. CHAI, with UNITAID funding:

Decreasing prices on two key ARVs, tenofovir and efavirenz, will lead to a savings of $1.3 billion over the next five years. CHAI estimates that $430 million of the savings on these two drugs can be directly attributable to CHAI's work on decreasing costs of manufacture and increasing competition in the marketplace.

Over the next 5 years, $90 – 130 million will be saved on a key new second line regimen (tenofovir, lamivudine, atazanavir and ritonovir). CHAI estimates that $70-95 million of the savings on this combination can be directly attributable to CHAI's work.

In addition to the direct savings highlighted above, CHAI's work benefits other organisations indirectly. For instance, when CHAI conducts its supplier negotiations in December and announces its prices in March; these prices become reference prices which SCMS (procuring on behalf of PEPFAR) and Medicines Sans Frontieres try to duplicate. So others are able to catalyse on CHAI's negotiations.[27]

In 2010 Waning et al (Globalization and Health) expanded on the factors which appear to be correlated with prices, including demand and competition-shaping effects of WHO treatment guidelines, quality assurance policies and pooled procurement strategies of funders. Although these studies have shown that individual country order volume is not always correlated with price and other studies (e.g. Seoane-Vazquez, et al Health Policy and Planning 2007) have shown that pooling volume across countries does not necessarily result in lower prices for individual countries, it would be a mistake to conclude[28] that volume and price are never correlated or that pooled procurement never achieves lower prices. There is a difference between the market leverage possible with individual country volumes versus the market leverage one can achieve by pooling volumes across countries. Other things being equal, the latter has more potential to achieve price reductions,

[26] With the exception of certain UNITAID-financed commodity categories, where CHAI does serve as procurement agent

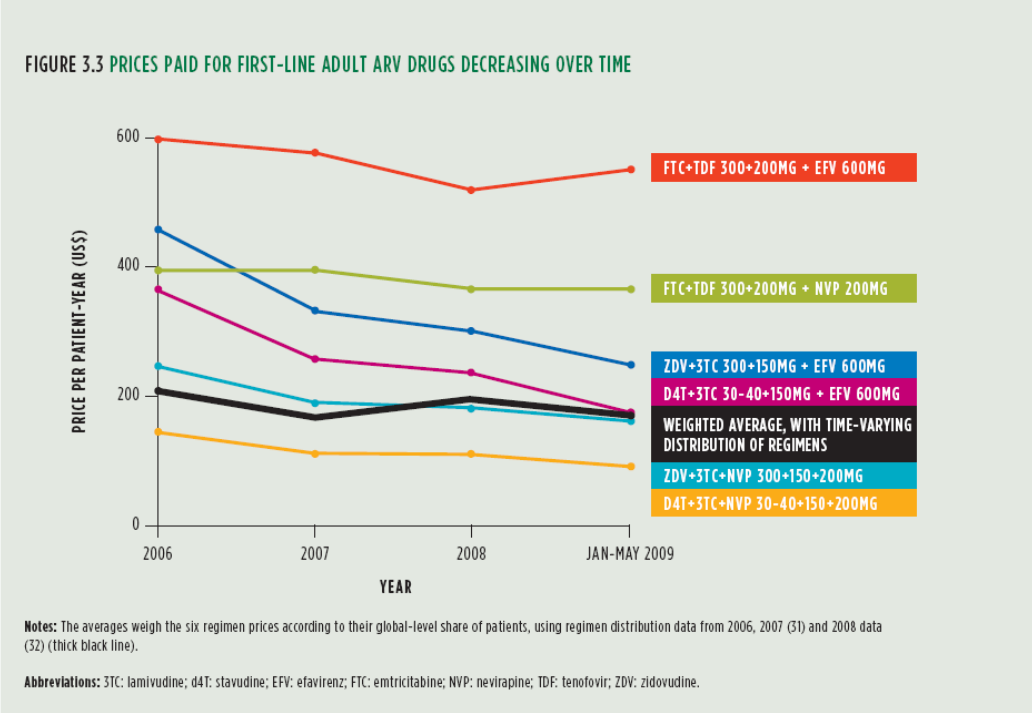
[27] Paolo Meireles, UNITAID Secretariat, personal communication

[28] As some have done, for example: http://www.aidsmap.com/page/1434627/

though of course this depends on how transparent and well managed the procurement process is overall.[29]

The overall price tag of ARV treatment is also influenced by the mix of ARVs countries are deploying. Global Fund grant funding has historically been distributed to more than 100 countries, each making independent purchase decisions. The sheer increase in funding amounts certainly had an impact on volumes and producer economies of scale and generic producers entered the market in droves, contributing towards significant price decreases since the Global fund's inception (see prices 2006-2009 in Graph 7).

Graph 7: ARVs prices paid by GF grantees 2006-2009



Slide source: Global Fund 2010: Innovation and Impact

However, despite the decreasing price of individual drugs, average cost of ARV treatment funded through GF grants between 2006 and 2009 has remained relatively stable. This is due to the shift in mix of drugs used. Different regimens differ markedly in price so that overall ARV cost depends on the number of patients using each regimen. Between 2006 and 2009, GF grant recipients used the more effective, and more expensive, efavirenz and tenofovir-based regimens and have begun phasing out the use of stavudine (d4T). (Global Fund 2010: Innovation and Impact Report).

As opposed to vaccines, ACTs, ITNs and TB medicines, ART is a repeated lifetime purchase, therefore achieving cost savings on ARV prices certainly needs to be a VFM priority.[30] In the Global Fund's 2010 performance indicators, there is the goal to

[29] Prices achieved through pooled procurement are influenced by a range of factors such as precise specifications being tendered, timing and size of the order, payment terms, overall demand and supply, cost of production, income level of the recipient countries, and competitive considerations.

[30] Although it should be noted that non-drug costs are at least 65% of overall ART delivery costs (Global Fund 2010 Innovation and Impact). Although beyond the scope of this study, a drive for cost-efficiency of non-drug related costs must consequently go along with a focus in achieving value for money in overall ART.

improve first line ARV prices by 5%. The baseline is $188, which was the overall median price of commonly used drug regimens for all countries with Global Fund programmes in 2008.

The number of patients currently receiving ART with GF grant money is 2.5 million. (The Global Fund 2010 Innovation and Impact Report). Given estimates that UNITAID funds more than 90% of second line patients, it is assumed that 97% of GF patients receiving ART are on first line ARVs. Assuming a 5% savings on treatment costs for 2.43 million patients, allowing these patients to be treated with a regimen that costs $178 instead of $188, the annual savings would be $24.3 million USD.

There has been a view that even greater price reduction could be achieved if grant recipients pooled their collective volume to increase their buying leverage; as previously noted, the GF's VPP was established towards that aim and certainly there is evidence to support the effectiveness of such a strategy in other commodity sectors like first line TB drugs and vaccines. However, as of January 2010, only 9% of the value of orders processed through VPP have been for ARVs, so VPP's influence on this product category will be limited if this situation remains.

Assuming the $24 million USD worth of ARVs procured though the VPP had been purchased at a 5% lower price, the savings would have amounted to $1.26 million USD.

VPP offers the example of Macedonia as a success story; national procurement would have led to a cost more than 4 times the initial grant budget, however VPP was able to procure ARVs at two-thirds of the prices in the grant budget. As the amount spent was $17,918, the savings would have been $90,000 USD. (If 18K is 2/3 the grant budget then the grant budget was 27K and 4x 27K = 108K. 108K minus 18K eventual spend equals a 90K savings)

UNITAID and PEPFAR have remarkably different strategies, versus GF, when it comes to ARV procurement. PEPFAR's procurement agent, SCMS, is credited with securing better purchase prices on 72% of its first line ARVs and 40% of second-line ARVs compared with other selected benchmarks, pricing sources and buyers. (such as GPRM, MSF and CHAI respectively) SCMS achieved these savings by "purchasing generic medicines whenever possible, pooling procurement, such as consolidating multiple orders to buy in larger volumes, and establishing long-term indefinite quantity contracts with manufacturers, thereby leveraging lower prices through bulk purchases." (PEPFAR press release Jan 20, 2009) SCMS signs indefinite quantity[31] contracts with two manufacturers for each ARV, bringing prices down through competition between the two and ensuring supply security by having more than one supplier.

Like PEPFAR, UNITAID also aggregates demand and purchases paediatric and second-line ARVs in bulk through its partnership with CHAI. These product sectors are relatively less mature versus the fist line ARV market and UNITAID is the dominant financier, so changes in these markets along any of the market shaping dimensions can be largely attributed to UNITAID's and CHAI's influence. (See Box above for specific, quantified impact).

Another market shaping intervention has been the development of price information databases. If made publicly available and user-friendly, these have the potential to

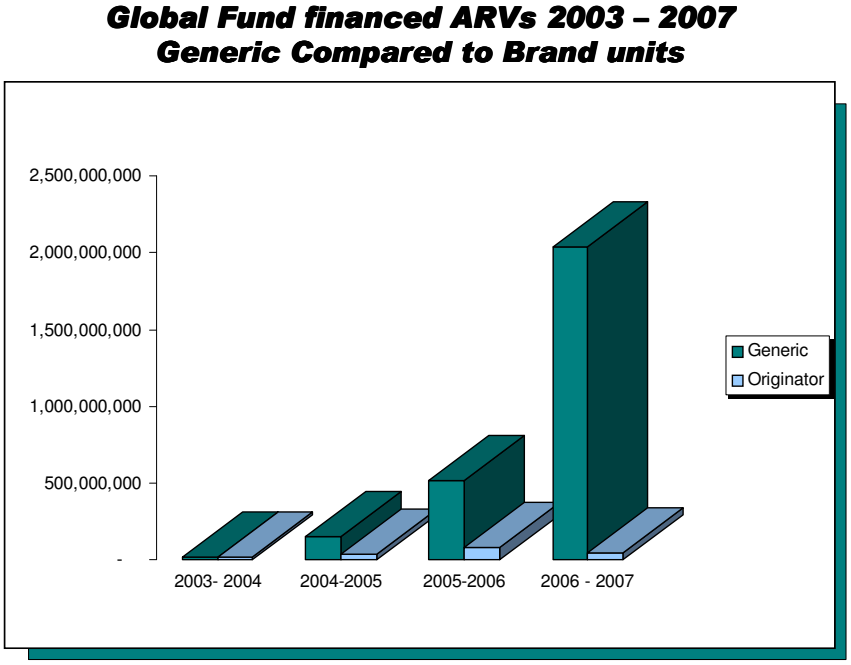
[31] Essentially a framework contract whereby the supplier commits to supplying certain volumes at pre-defined prices; usually price/volume ranges are offered, with prices at minimum and maximum volumes specified.

increase leverage of buyers in a similar way to pooled procurement. GF grant recipients are required to report prices paid for ARVs in the GF's Price and Quality Reporting System (PQR) which is linked to the global price-reporting system hosted by WHO. To the degree that the information reported is accurate and users are able to decode it, these databases may facilitate price comparisons and increase leverage of grant recipients to negotiate prices. DFID has been funding Boston University to clean this data and complete it with data from other public procurement sources. This has usefully allowed Boston University to interpret the price determinants of ARVs and publish the results in the paper references herein. UNITAID will fund the continuation of such work, including making the data publicly available, which will allow a wider range of users to interpret and make use of the data.

Supply Security

The substantial increase in financing, irrespective of deliberate market shaping activities, has resulted in a diversified supplier base, as evidenced by Graph 8 below and relative to the counterfactual world without the Global Fund.

Graph 8: The Rise of Generic Suppliers of ARVs



Source: Analysis conducted by Brenda Waning and Manjusha Gokhale, Boston University School of Public Health

Similarly, Waning et al 2010 show a direct relationship between eligibility for PEPFAR funding, demand scale up and new market entry. The same paper reveals the market consolidation and price reductions achieved through PEPFAR's procurement methods and highlights the risks when a greater concentration in buyers through pooled procurement results in a greater concentration of suppliers. As is evident from the vaccine section reviewed herein, pooled procurement strategies are numerous and need to be tailored to achieve a balance between supply security and sustainable pricing.

Quality

The GF requires that ARV products are certified by the WHO PQP or a SRA. Suppliers to PEPFAR must receive FDA "tentative approval" - a process to allow ARVs produced anywhere in the world to be FDA reviewed to assess quality standards and subsequently cleared for purchase under PEPFAR. Waning et al 2010 concluded that the three-year wait to use PEPFAR funds for the most commonly-used FDC (3TC/NVP/d4T) caused delay in the maturation (volume increase, supplier entry and consequent price reduction) of the market for that product, revealing the tension that can exist between quality requirements and price reduction.

Availability

With the exception of Mozambique, Zambia, Nicaragua and Niger, most of the ARV orders processed through VPP have been small quantities (less than $1 million per order). In the Macedonia case previously mentioned, the country had problems getting a response from international procurement agents due to the small order volume. In addition, a substantial part of VPP orders (approximately 50%) were emergency orders (Mozambique and Zambia). It would seem that the major benefit of VPP is this product category has been primarily improved product availability at the level of individual countries.

Product Innovation

WHO Treatment Guidelines can influence incentives to develop new compliance-enhancing FDCs. Waning et al 2010 hypothesize that the proliferation of 20-some treatment regimens in WHO's 2006 guidelines may have reduced incentives for manufacturers to develop FDCs of newer regimens. The 2009 guidelines have streamlined the number of recommended first line regimens to six, which may serve to consolidate demand and enlarge markets, so it is hoped that incentives are improved for producers to develop FDCs of the newly recommended regimens.

Second line ARVs: In partnership with CHAI, UNITAID has encouraged the manufacture of 6 paediatric regimens and 7 second-line HIV formulations.

Paediatric ARVs: Before the UNITAID/CHAI intervention, paediatric ART required 16 bottles of foul-tasting, single dose syrups per month, costing $200 USD per year. Now, there are six versions of a three-in-one paediatric tablet, taken 3 times per day, and costing $60 USD per year. For the same amount of money, 3 children can be treated instead of 1, and with a superior product promoting compliance.

(UNITAID factsheet)

Conclusion

In summary, it is the overall catalytic effect of GF financing, rather than any deliberate GF supply strategy, which has resulted in market changes. CHAI negotiations have been the most instrumental influencer of price. The impact of the VPP on ARV supplies remains to be seen.

UNITAID has taken a more deliberate market shaping role, providing goods instead of funds, creating new markets where it is the dominant funder, and focusing directly on catalysing market changes. PEPFAR's impact as a market shaper was delayed, due to the wait for the FDA tentative approval process to certify generic FDC quality and eligibility for funding. However, it is a major funder of first line ARVs and has certainly contributed to volume growth and market maturation of the first line drugs.

WHO's treatment guidelines are influential. As noted, the range of possible ARV combinations recommended needs to factor in a balance between the individualised needs of countries and the market impact effect of shaping and consolidating demand around a smaller number of drugs, which would lead to higher volumes and enhanced predictability in production planning.

3.4 Vaccines

The GAVI Alliance is a global health partnership working to save children's lives and protect people's health by increasing access to immunization in poor countries. GAVI accelerates access to existing underused vaccines, balancing supply security, affordable pricing and country preference of presentation. Finance is provided for uptake of new and underused vaccines as well as immunization systems strengthening needed to facilitate uptake. Countries receiving GAVI grants are obligated to obtain their vaccines from UNICEF, GAVI's designated procurement provider.[32] During Phase I (2000-2005) GAVI funded vaccines against three diseases, Hib, HepB and yellow fever – where supply has been dominated by western R&D based producers. Between 65% - 75% of GAVI's funds are used to finance these newer vaccine technologies (minus a small country copay). The remaining 25% - 35% is spent on immunization services strengthening, injection safety support and (in more recent years) health systems support.[33]

Prices

HepB combination vaccines

In 1992, WHO had recommended the introduction of HepB into EPI programmes. Prices for monovalent HepB had begun to decline by the early 1990s due to the efforts of the International Task Force on Hepatitis Immunization, who began the push in the 1980's to have HepB included in developing country immunization schedules and to facilitate the technology transfer to emerging manufacturers.[34] The increase in global demand, coupled with the emergence of new suppliers, especially those from Korea and India, created a textbook case of a maturing product with price decreases. Prices in 1993 were more than $2.00 per dose, falling to $.75 by 1997[35]. However, $.75 per dose was still much higher than the other vaccines in the EPI schedule in developing countries - in the range of $.06 to $.10 per dose for measles, oral polio and DTP – consequently uptake was still challenging.

While prices for monovalent HepB continued to decline, prices for the newer HepB vaccine combined with DTP (the "quadravalent" presentation preferred by GAVI countries) increased from $1.10 per dose in 2001 to $1.29 per dose in 2006[36]. It was not until the tender of 2007-2009 that price reductions were seen. The weighted average price declined from USD 1.21 to USD 1.29 for the 2004-2006 period to USD .76 – USD .71 for the 2007-2009 period. Total savings are summed in bold in the table below[37].

[32] Countries are exempt from using GAVI's procurement if they can procure the same quality level for the same price using domestic procurement systems.

[33] See page 9 of GAVI Alliance Progress Report 2007 for past expenditure breakdown and Page 10 of GAVI Alliance Progress Report 2009 for anticipated expenditure breakdown

[34] Immunization Financing in Developing Countries and the International Vaccine Market. 2001. Asian Development Bank. P 43.

[35] Pg 65, Evaluation of the GAVI Phase 1 Performance (2000-2005) Abt Associates

[36] 12th GAVI Board Meeting – 9-10 December 2003, Geneva pg. 17

[37] GAVI Alliance and Fund Board Meeting 11-12 May 2007. Doc#AF-8 Vaccine market development. Page 10.

DTP-HepB (10 ds vials)	previous awards	2007	2008	2009
Updated demand quantity (doses)		34,987,721	65,714,943	67,291,875
No of suppliers awarded	1	3	2	2
Total award quantity (doses)	44,500,000	26,300,000	34,100,000	19,500,000
Weighted average price	1.29	0.75	0.7	0.71
Total vaccine financed	57,405,000	19,725,000	23,870,000	13,845,000
award multiplied by 1.29 price		33,927,000	43,989,000	25,155,000
Annual savings versus 1.29 price		**$14,202,000**	**$20,119,000**	**$11,310,000**

Hib combination vaccines

The price of Hib vaccines had also dropped substantially prior to GAVI's emergence, from $5.00 per dose in 1997 to $2.50 per dose in 1998. Like HepB, Hib vaccine introduction was challenged also by its high price - $2.60 - $3.50 per dose throughout GAVI Phase I – but additionally, by lack of recognition of the burden of disease in developing countries.

The pentavalent DTP-HepB+Hib vaccine combination was ultimately the preferred GAVI product, as it allowed immediate introduction into existing delivery systems, minimising cost of introduction and delivery. However, six years lapsed between the beginning of GAVI and the emergence of a second supplier of the expensive DTP combination (pentavalent) vaccine, made by Glaxo Smith-Kline. Two new pentavalent products became licensed between 2000 and 2005, however, only one pentavalent product (GSK's) was pre-qualified during GAVI Phase I, and pre-qualification was a requirement for purchase by GAVI under the UNICEF procurement system. Consequently, GAVI was left with a monopoly supply situation - GSK as sole tetra/pentavalent Hib supplier at high prices. GSK's price was about $10 per treatment course (ranging from 3.50 to $3.65 per dose in the 2001-2006 time period[38], whereas the price of the other pentavalent products (licensed but not pre-qualified) would have been about $5 per treatment course. Manufacturers of the tetravalent (DTP+Hib) were reportedly frustrated because their vaccine was readily available as an alternative, but countries' preference for the pentavalent vaccine was supported by GAVI.[39]

[38] 12th GAVI Board Meeting – 9-10 December 2003, Geneva pg. 17

[39] Pg 67, Evaluation of the GAVI Phase 1 Performance (2000-2005) Abt Associates

Box 2: Case study - How product acceptability (presentation and perceptions of quality) can come into conflict with achieving lowest prices

UNICEF's ability to achieve efficiencies in procurement is only part of the equation, when looking at GAVI's strategic goal of improving vaccine affordability. A key component is choice of product and product specifications, a factor UNICEF does not dictate. Rather, GAVI short-lists which technologies it will fund, based on the investment case process, and countries make choices within that short-list. Several GAVI evaluations have criticised this aspect of GAVI's contribution.[1]

GAVI has been faulted for choosing the monopoly supplied, tetravalent Hib vaccine, when it could have chosen the competitively supplied monovalent or bivalent equivalent. However, GAVI justified this decision based on the rationale that 'programmatically, countries did not want the monovalent because they did not want multiple shots'. Similarly, countries preferred the 10 dose vial rather than the 5 dose vial for yellow fever. One study concluded this preference was only because the 10 dose vial was produced by a brand-name pharmaceutical company whereas the pre-qualified 5 dose vial was produced by an emerging market manufacturer without such an international reputation. Thus the conclusion was that GAVI could have usefully facilitated acceptance of emerging market products and of the WHO pre-qualification process at country level. [1]

If we refer to the VFM framework presented earlier, then the entire costs per effective use and per health impact would need to be considered in determining VFM. Thus not only cost of the vaccine, but also cost of delivery should be considered, the increased acceptability of one rather than multiple shots may have facilitated uptake and use, and the quality requirements facilitate health impact, the final outcome in the value chain.

UNICEF is contracted to manage GAVI's procurement, so an evaluation of GAVI's price impact naturally entails an evaluation of GAVI and UNICEF's joint impact. GAVI's contributions in this respect were criticised in a 2005 review:[40]

- Demand forecasts for GAVI markets had a wide range (NB: Much uncertainty surrounded the timing of actual country uptake, which was a country decision, not a GAVI decision).
- GAVI had not communicated which vaccine presentations it would prioritise going forward, so suppliers were developing three presentations
- A 2006 evaluation[41] also concluded that "there are many more tools used in modern procurement that UNICEF is not yet fully using, which could be used to accelerate market maturation, including risk sharing, multi-year contracts, etc."

Similarly, a 2008 evaluation recommended that "The GAVI Board should commission a study of innovative ways to structure procurement of new vaccines (other than short term fixed price contracts) that may be more advantageous over the long term".[42]

In the 2005 review, GAVI was advised to:

- Build credible demand (evidence of burden of disease, develop reliable financing (incl. through IFFim and AMCs);
- Make transparent which vaccines GAVI will prioritise (which presentations, price/volume expectations and over what timeframe, set clear criteria for awarding contracts); and

[40] Global Vaccines Supply: The Changing role of Suppliers, Boston Consulting Group, Presentation to External Stakeholder Advisory Board Meeting. Sept 13, 2005.
[41] "Mapping the Bigger Picture of Immunization" Report for GAVI, HLSP 2006.
[42] Abt Associates 2008

- Manage the market (develop a supply strategy) for each priority product (address barriers to pre-qualification, address potential regulatory issues, provide access to technical resources of information, provide technical or financial support).

In recent years, UNICEF has improved its forecast accuracy, and has tailored its procurement and supply strategies, with oversight from new 'Procurement Reference Groups' (PRG) focused on each GAVI funded vaccine, and addressing some partners' views that 'UNICEF could be more successful in achieving lower prices in monopoly supply situations'. However, the GAVI Phase II Evaluation concluded that GAVI continues to miss opportunities to improve affordability: "GAVI has not been sufficiently proactive in understanding the nature of price drivers for its key vaccines or in working with suppliers to maximise price reductions through explicit strategies."[43]

Supply security

GAVI's main contribution as a market shaper has been in providing a substantial funding stream, an important signal to industry that there was a significant, long-term, reliable market for these products. GAVI created the market for Hib combination vaccines in developing countries, and can be attributed with accelerating the growth of the combination HepB vaccine market. It also provided immunization systems and health systems strengthening funding, to enable vaccine uptake. The result was encouragement of market entrants, as evidenced by the number of vaccine products pre-qualified or in the pre-qualification process. From 2000-2005, the number of manufacturers producing pre-qualified products suitable for the GAVI market increased from 10 in 2000 to 24 by 2005[44]. Support for a pro-competitive environment has been shown to be supportive of price reduction, supply security and increased innovation[45] and this, in turn, enhances consumer welfare. So in providing an environment supportive of new market entrants, GAVI has increased the potential for longer term price reduction.

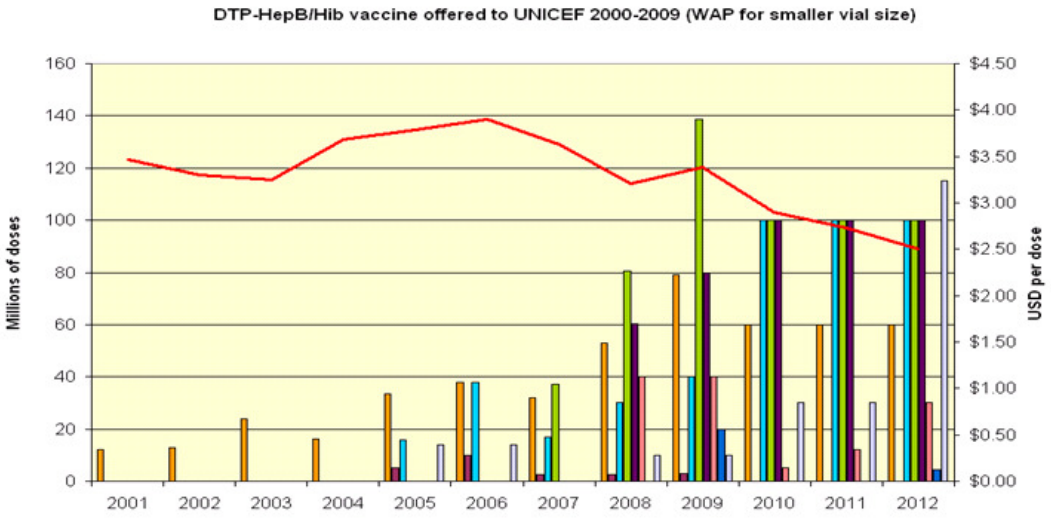
However, despite diversification of the overall vaccine supplier base during the first 6[46] years of GAVI, there remained only one pre-qualified product for each of the two vaccine combinations GAVI countries most demanded, DTP-Hep B and pentavalent DTP-HepB+Hib. GAVI's preference for the use of combination vaccines caused a sharp rise in the demand for the pentavalent vaccine, at a time when capacity was already fully utilised supplying wealthy market demand. This resulted in a supply shortage. The GAVI Phase I Evaluation concluded "both industrialised manufacturers and other GAVI partners agree that there were missed opportunities for dialogue in the early years of GAVI that contributed in the ultimate shortage of pentavalent vaccine." In a 2006 evaluation[47], it was noted that The Serum Institute could have supplied the Hib vaccine much earlier and at substantially lower prices relative to the sole supplier – GSK – if GAVI been willing to commit upfront payment or make a promise to buy. This would have allowed Serum to expedite development and pre-qualification. This was discussed with GAVI, but it never materialized.[48]

[43] GAVI Second Evaluation Report, 13 September 2010. CEPA LLP and Applied Strategies. Page 71.
[44] Pg. 67 Evaluation of the GAVI Phase 1 Performance (2000-2005) Abt Associates
[45] As reviewed in pages 13-15 of Grace, C. The Effect of Changing Intellectual Property on Pharmaceutical Industry Prospects in India and China Considerations for Access to Medicines, A paper for the Department for International Development, 2004. http://www.dfid.gov.uk/pubs/files/indiachinadomproduce.pdf
[46] According to the page 21 of the GAVI Phase 1 Evaluation, there was only one supplier for these 2 products during the first 8 years of GAVI. However, expert interviews have revealed that Crucell started supplying in 2006, so there were only 6 years of single supply.
[47] "Mapping the Bigger Picture of Immunization", Report for GAVI, HLSP, 2006.
[48] In GAVI's experience, manufacturers are not entirely realistic on the timelines for pre-qualification.

Clearly the "pull" of GAVI funding must have sent a strong signal of demand credibility, yet it still took much longer than anticipated for alternative suppliers to become pre-qualified. The GAVI Phase I Evaluation concluded that GAVI had been overly optimistic and unrealistic in its assumptions about the timeframe for new supplier entry.[49] The Hib vaccine used a novel and more complex technology – conjugate technology - which slowed the pace of new manufacturers entering the market, especially emerging market manufacturers. There are significant costs and lead times for new vaccine capacity to be put into place and approved and it would have made sense for suppliers to wait and see if GAVI would have long term funding before investing in new capacity for GAVI specifically. Nonetheless, the Phase I Evaluation concluded that better results might have been achieved sooner if GAVI had engaged emerging suppliers earlier, had produced rigorous forecast that manufacturers could rely upon, encouraged use of alternative vaccine presentation, encouraged UNICEF towards multi-year contracts earlier, and invested additional resources in working with WHO to improve its pre-qualification process.[50]

Emerging market manufacturers have now finally introduced pre-qualified variations of the Phase I supported vaccines and the market has transitioned and matured with higher competition and lower prices.

Graph 9: Pentavalent market development



Slide source: UNICEF

NB: Slide shows all offers to UNICEF – pre-qualified and non-pre-qualified suppliers

UNICEF is actively managing the number and allocation to suppliers based on market demand and supplier availability relative to market demand and tailors its procurement strategy accordingly. For the 2010-2012 tender period, UNICEF has developed four different tender strategies, reflecting the market realities and consequent priorities for 4 different product categories seeking to achieve/ ensure vaccine security in the various markets:

- Traditional EPI vaccines: objective was to maintain supply security so long term agreements (LTAs) were made for 3 years, committing specific quantities (with the exception of Tetanus Toxoid vaccine, where the objective is to broaden the

[49] Page 68, Abt Associates

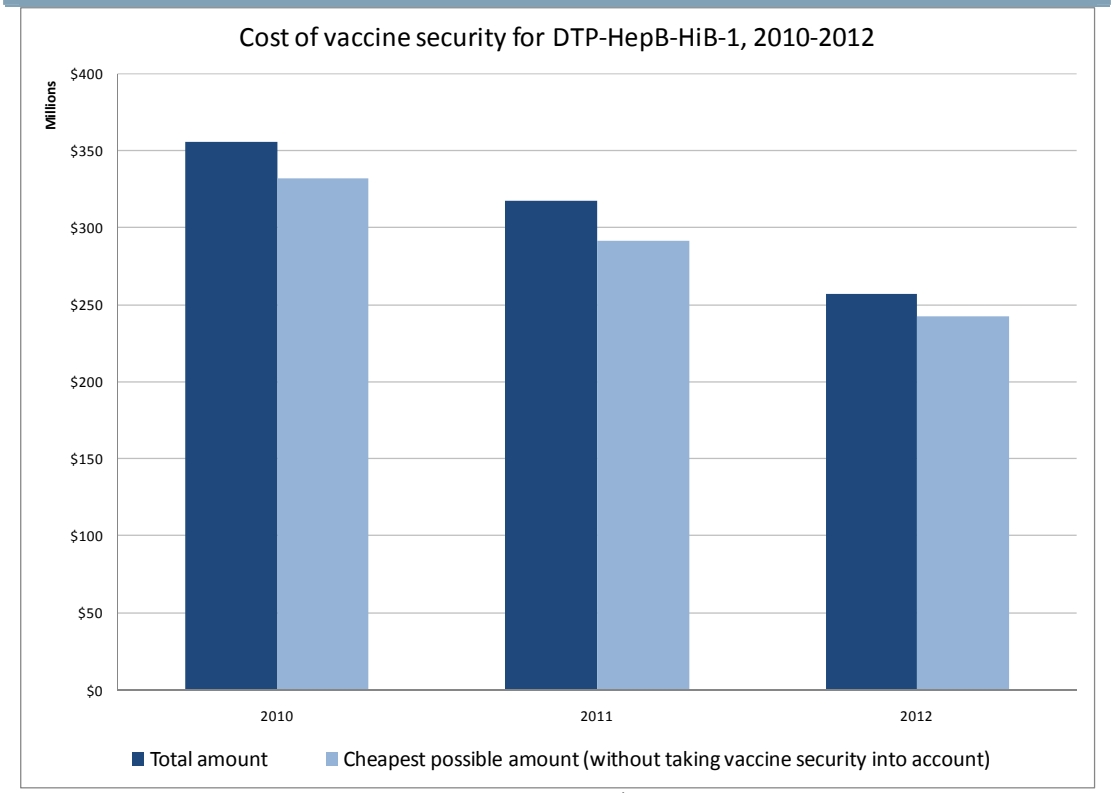
[50] Page 68, Abt Associates

supply base so some forecast quantities were left un-awarded for 2011 and 2012) based on the market knowledge that there was another manufacturer soon to achieve pre-qualification

- Pentavalent: The priority was price reduction, so UNICEF opted to reserve a percentage of projected demand in each year to put out for subsequent competition – 8% in 2010, 28% in 2011, and 40% for 2012.
- Measles: There are 3 suppliers and a heavy reliance on 1 of 3.[51] The priority was to encourage new entrants, therefore relatively large volumes were left un-awarded for 2011 and 2012 in an effort to broaden the supply base.
- Yellow fever: The tender was tailored to allow for a situation where future funded demand is unknown. Quantities of 50m and 90m doses were left un-awarded for 2011 and 2012 preventative campaigns.

As noted, UNICEF sometimes splits awards amongst several manufacturers, some having higher prices than the lowest bidder. Graph 10 below illustrates what UNICEF calls the "vaccine security premium" which resulted when awards were split in the most recent measles and pentavalent tenders. If UNICEF had been focused on achieving the lowest price, while neglected supply security, then 91% to 100% of the total award volume would have been allocated to a single manufacturer, utilizing 100% of its capacity, and requiring it to scale up by a factor 5 compared to current production level. The supplier is no longer pre-qualified, highlighting the reality of the risk.

Graph 10: Illustrating the "vaccine security premium"



NB: DTP-HepB/Hib (1): Vaccine Security Premium = US$60M (6%) of the total recommended award for 2010-2012.
Slide source: UNICEF

[51] Reliance on a concentrated supply base is especially problematic in vaccines, since variable yields, batch failures and slow regulatory release are inherent difficulties with the production of biological products.

Innovation

GAVI has been in the centre of several innovative programmes and financing experiments, which have the intention of shaping the market in a positive way. For example, GAVI has invested in ADIPs – Accelerated Development and Introduction Plans, now AVI (Accelerated Vaccine Introduction Initiative). This has been focused on understanding the disease burden from rotavirus and pneumococcus, building the demand (e.g. demonstrating the disease burden) and building the supply base (working with producers to develop the target product profile required to meet developing country needs) for the next generation of vaccines.

GAVI has started to receive frontloaded funding for immunization through borrowing on the bond market. The theoretical advantage versus traditional grant funding is an acceleration of market maturity - frontloaded funding fuelling country confidence to increase in volume uptake/demand, resulting in increased economies of scale for producers, resultant decreased costs, and (in the environment of competition or bilateral cost-plus negotiations) passing those cost savings onto purchasers in the form of reduced prices. One could theoretically foresee the increased predictability and frontloading features of IFFim to enable an increased range of contracting options for UNICEF, increased ability to predict demand and which vaccine presentations would be purchased. We do not yet know whether these theoretical benefits have been realised. An evaluation of IFFim is underway at present.

GAVI also houses the Advanced Market Commitment initiative, which is expected to accelerate the market entry of a pneumococcal vaccine(s) with the serotypes and other product features tailored to meet developing country needs.

Discussion/future challenges

As GAVI looks towards introducing even newer vaccines like rotavirus, pneumococcal and HPV, GAVI will again be in monopoly and duopoly supply situations, where innovative financing methods like IFFim and AMCs are expected to produce benefits. Whether and how these theoretical benefits are realised remains a key question going forward.

Annex 1

Organisations Consulted

1. IMS
2. Global Fund
3. World Health Organisation
4. UN Special Envoy on Malaria
5. Net Mapping Project
6. BMGF
7. UNITAID
8. UNICEF
9. MMV
10. DFID
11. TB Alliance
12. CHAI
13. PSI
14. Novartis
15. Clarke Mosquito
16. Cipla
17. Matrix
18. Panacea
19. Serum Institute
20. Indian Manufacturers Association
21. MSF

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