The public health challenge

Anil Soni and Ira Magaziner outline the work of the Clinton Foundation HIV/AIDS Initiative…

Two years ago, the William J. Clinton Foundation signed agreements with 10 manufacturers to lower the prices of HIV/AIDS antiretrovirals (ARVs) and diagnostics. We often receive questions about how suppliers were able to lower their prices so dramatically and what these agreements have achieved in practice. The article below is intended to answer these questions and highlight the challenges still ahead to keep treatment affordable.

The price of ARVs is critical to the reach and sustainability of any HIV/AIDS treatment programme. When the Clinton Foundation HIV/AIDS Initiative (CHAI) began its work, partner governments asked for assistance in securing the supply of high quality ARVs at the lowest possible prices. Our response was to apply business competence to a public health challenge. The supply of ARVs is a for-profit enterprise. Treating it as such allowed CHAI to work with – rather than against – manufacturers to optimise outcomes for patients.

Approach

For generic manufacturers, the market for ARVs just a few years ago was small and fragmented. Economies of scale common to pharmaceutical production could not be realised, sales volumes were unpredictable and purchasers often paid late or defaulted altogether. Disorganisation in the market made it impossible for companies to plan for efficient production, and payment risk contributed to unnecessarily high costs.

In 2002, CHAI began working with governments in Africa and the Caribbean to scale-up access to ARV treatment. Based on the plans we helped them to develop – and would help to implement – we were confident that ARV sales volumes would increase quickly. This insight gave us credibility with manufacturers, whom we approached with a commitment to stimulate demand and improve procurement practices in partner countries. Together with these high quality suppliers, we set out to map the manufacturing process and its component costs (Fig. 1).

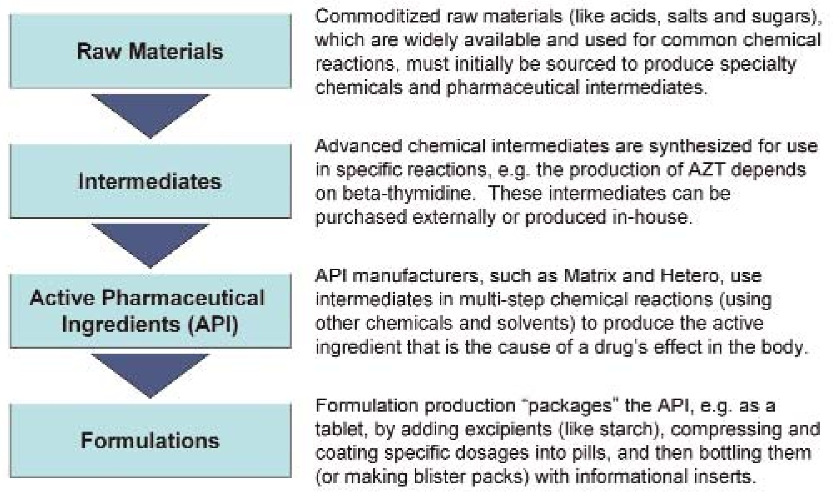
The majority of final formulation costs are in the purchase or in-house production of active pharmaceutical ingredients (APIs). Production costs of APIs – in addition to the smaller cost to manufacture formulations – are dependent on scale. Larger orders of chemical intermediates yield better prices; direct expenses such as power and labour are minimised when chemical reaction chambers are larger and filled to capacity, and when production lines are run continuously, rather than on a batch-to-batch basis; and indirect expenses add up to less per unit when more units share them. Thus, the increased volumes we anticipated as treatment programmes rolled-out were directly linked with significant savings in the per person per year cost of ARVs.

More savings were possible. Recognising HIV/AIDS as a global health emergency, manufacturers took a bold step by committing to cross-subsidise most standard overheads by sales of other products and to retain only nominal margins for ARVs. Their ongoing sale would be a low margin but high volume business (which would remain sustainable so long as prices covered all direct costs plus depreciation and cost of capital while providing for a margin).

The third source of savings came from ‘forward pricing’ – pricing based on costs associated with volumes that we knew would not be realised for up to three years. API suppliers, in particular, were able to do this because they had confidence that, in addition to the volume-based manufacturing savings we assumed, they would be able to achieve higher yields over time (as they gained experience) and therefore require fewer raw materials. Knowing that costs would fall, suppliers agreed to forward pricing to help stimulate demand and to gain market share.

On the basis of these savings, CHAI signed agreements in October 2003 with five suppliers specifying prices for nine formulations of the most common ARVs: zidovudine (AZT), lamivudine (3TC), stavudine (d4T) and nevirapine (NVP). Partner API suppliers, Matrix and Hetero, would supply at or below the specified prices when selling to partner formulators. The partner formulators – Cipla, Ranbaxy, Hetero and Aspen Pharmacare – would sell at or below the specified formulation prices when selling to CHAI purchasers (at the time, a dozen countries that represented a third of HIV prevalence in Africa and 90% of prevalence in the Caribbean). Formulation prices were ‘free

Figure 1
Pharmaceutical Production Process



on board' (FOB) – meaning that shipping, handling and insurance would be additional.

What did CHAI and its purchasers agree to in return? The agreements require prompt and secure payment terms, such as letters of credit. Furthermore, they reflect principles of sound procurement, each tied to assumptions about cost savings. These include: aggregated national orders; ongoing forecasting of product volumes; reliance on international quality standards such as World Health Organization (WHO) prequalification or US Food and Drug Administration approval; expedited national registration based on those standards; secure distribution of product in country (to avoid leakage into high income markets); and, finally, movement towards the use of multi-year tenders and splitting high volume orders across two or more suppliers.

The importance of these practices was reinforced in 2004 as CHAI broadened access to its prices, following agreements signed with partners including the Global Fund and the World Bank. Countries were added on a case by case basis after the government of each potential purchaser signed a memorandum of understanding committing to the practices above. This reassured partner suppliers that the prices to which we agreed would be sustainable across a larger market.

Outcomes

For the most common three drug treatment regimens, CHAI prices represented a reduction of more than 50% compared to the lowest priced, high quality generic alternatives at the time, and 75% compared to branded equivalents (Fig. 2). Countries purchasing under CHAI agreements could immediately treat two to three times as many patients with a given set of resources. Our prices were available to low and middle income countries alike, consistent with national and international law. The impact in middle income countries, such as those in the Caribbean, was especially dramatic.

In the last two years, access to these prices has been extended to 48 countries, representing 70% of people worldwide living with HIV. To date, 25 countries have completed orders for a total purchase of more than 200 million pills, so that more than 180,000 patients on treatment today are benefiting from medicines purchased under our agreements.

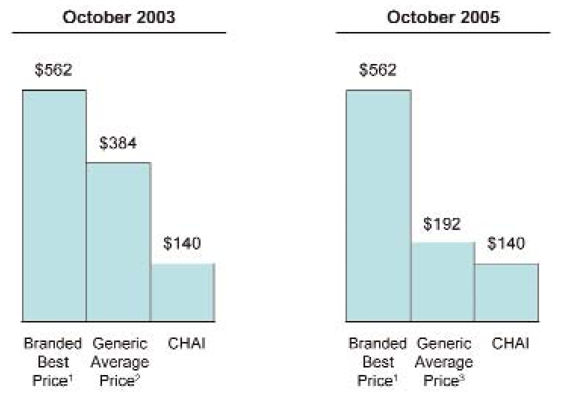
We have confirmed that prices paid on these orders hold true to our agreements. Actual purchase prices include costs for freight and, in some cases, fees for procurement agents – both on top of standard FOB rates. Procurement agent fees have been excluded where relevant based on a 10% standard (consistent with what UNICEF and the International Dispensary Association charge clients to cover their costs). The result? Actual prices for orders made under CHAI agreements have, on average, been within 3% of the price ceilings – consistent with expected overheads for shipping, handling and insurance.

The prices set by CHAI partner suppliers had a ripple effect on the market. The agreements accelerated price decreases for first line ARVs, and their 'cost-plus' framework has ensured that all high quality manufacturers price at the lowest possible rates. Market rates are now more consistent with CHAI ceilings – the average price listed by suppliers for the most common fixed dose combination is within 27% of the CHAI ceiling (Fig. 2).

Beyond list prices, there is increasing transparency in the market of actual prices paid by purchasers following the completion of orders. According to prices reported to the WHO by low income countries, purchase prices under our agreements are, on average, 20% lower than those outside our agreements. Not surprisingly, the difference is more pronounced in middle income countries, which are paying more than twice as much when buying outside our agreements.

The price of medicines is not the only factor driving the cost of treatment. CHAI partnered with the world's leading HIV/AIDS diagnostic suppliers to lower the laboratory costs associated with treatment. Through agreements signed in January 2004, Becton Dickinson and Beckman Coulter lowered the price of CD4 testing from an average of $15-20 per test to $3-5 (based on the use of high throughput instruments). Roche, Bayer and

Figure 2
ARV Price Comparison: 3TC+d4T(40)+NVP



1 As reported by the manufacturers and by Médecins Sans Frontières (MSF) in "Untangling the web of price reductions"
2 $384 was the weighted average price being offered to CHAI purchasers in October 2003. Prior to this, MSF, in its May 2003 pricing guide, reported the best prices offered by Cipla, Hetero and Ranbaxy as $301, $281 and $285, respectively.
3 Average price, per MSF's June 2005 pricing guide, of three suppliers currently WHO prequalified (Cipla, Hetero, Ranbaxy)

bioMérieux lowered the price of viral load testing by up to 80%. Given the frequency of testing and the number of patients involved, the immediate impact was substantial. Nearly two years later, the market once again reflects the vision of the manufacturers willing to accelerate price reductions: their prices are what countries now expect in Africa and the Caribbean.

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Challenges

It would be a mistake to assume that the current prices of ARVs are absolute, especially in light of cost pressures on suppliers. For instance, the supply of intermediates, often sourced from China, is a growing source of pressure as tougher environmental standards force some suppliers out of the market and others to raise prices. The prices of petroleum-based solvents are also increasing with the rise in oil costs. Formulators, for their part, are under strain as the US dollar weakens, given that their prices are listed in this currency.

Purchasers' procurement practices can also 'cost' suppliers more than expected if they are not consistent with those we assumed in modelling production costs. Purchasers who do not pay promptly risk suppliers charging more. Short-term tenders do not provide the predictability suppliers need to plan for long-term production needs or to achieve better pricing on large volumes of intermediates. Poor procurement practices can also have the negative effect of undermining competition. For example, countries that do not enforce strict quality standards create a skewed playing field for high quality suppliers, potentially forcing them out of the market if forced to compete with lower quality products (which are cheaper to make).

CHAI is working with suppliers to mitigate these pressures. For example, we are increasing our focus upstream in the production process, and in July signed our first agreement to secure ceiling pricing for five intermediates, supplied by Mchem, a Chinese manufacturer. We are also educating purchasers about how procurement practices affect price and helping them to improve local procurement and distribution systems.

In addition to the challenges associated with keeping first line ARVs affordable, countries are struggling to pay for increasing volumes of second line medicines. For any patient on treatment today, second line therapy is the natural and necessary next step to sustained clinical care; but this transition is a financial burden on national programmes, as second line treatment costs, on average, more than 10 times as much as the most common first line regimen. This is the best case scenario in the poorest countries of Africa, where patent holders offer the lowest access prices.

Access to ARVs in developing countries has expanded to more than one million people living with HIV. We must now follow through on our promise to keep them on these medicines while continuing to extend access to the five million more who need treatment today. This will be possible only if we can lower the prices of second line medicines, and CHAI is working with suppliers to do this in the coming months. What matters most as we do so is finding ways to harness the benefits of a well functioning market between committed manufacturers and competent purchasers. Their actions will pave the way for continued success.

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