



The Treatment Timebomb



Report of the Enquiry of The All Party Parliamentary Group on AIDS
into long-term access to HIV medicines in the developing world.

July 2009

“Reducing the costs of drugs could enable savings that could fund access to life-saving treatment for an additional one million people every year, even without new resources.”

DFID 'Achieving Universal Access'

'The UK's Strategy for Halting and Reversing the Spread of HIV in the Developing World' 2008.

Foreword

Photo: Tom Whipps



Dr Peter Piot

Director of the Institute for Global Health at Imperial College London; Former Executive Director of UNAIDS



David Borrow MP

Chairman, The All Party Parliamentary Group on AIDS

“This report from The All Party Parliamentary Group on AIDS reminds us that we not only need to stay focused on achieving the Millennium Development Goals on AIDS, but also on sustaining them. AIDS is with us for the long-term. The millions of people living with HIV need a lifetime of treatment, care and support. In laying bare the cost of a life-time of medicines the report is also a stark reminder of the importance of prevention.

Real political commitment to HIV means looking ahead and addressing problems before they become crises. ‘The Treatment Timebomb’ is an important wake-up call to those who think we can deliver on Universal Access in the long-term by just doing more of the same. Today’s low-cost HIV regimens will not be effective for everyone for a life-time and we have a responsibility to ensure that when they do stop working, people with HIV are not left to die.

The unprecedented challenge of HIV calls on us to be creative and bring together the best of what Governments, charities and the private sector can offer in terms of innovation, and push and pull incentives described in the report.

I congratulate the All Party Parliamentary Group on AIDS on this important report and hope you will join them in building the political momentum we need to deliver on our commitments to people living with HIV well beyond 2015.”

“This report is the culmination of an Enquiry by The All Party Parliamentary Group on AIDS. We have gathered information from as wide a number of sources as possible to ensure that our report presents a balanced picture and comes up with realistic recommendations.

An invitation to submit written evidence to the Enquiry was sent to all our supporter contacts, including hundreds of charities, businesses and individuals, in February 2009. This was followed by a parliamentary round-table event in March with experts and representatives of key institutions. Finally a cross-party section of the APPG made a short fact-finding visit to Geneva in April to interview the relevant UN institutions and the Global Fund for AIDS, TB and Malaria.

I would like to give our thanks to all of the organisations that contributed to the enquiry – they are listed on the back cover – and the many individuals who took the time to meet us. I would also like to thank the Ambassador of the UK Mission to the UN, Peter Gooderham, and his staff who helped organise our meetings in Geneva.”

Special thanks also to: Evan Harris MP, Neil Gerrard MP and Lord Norman Fowler.

The final report was compiled by Veronica Oakeshott, Policy Adviser the APPG.

If you would like any further copies of the report, please contact oakeshottv@parliament.uk

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A note about The All Party Parliamentary Group on AIDS

The All-Party Parliamentary Group on AIDS is a backbench cross-Party Group of MPs and Peers in the UK Parliament at Westminster.

Members of APPG on AIDS believe that HIV/AIDS is one of the most serious threats facing the world in the 21st century and that as Parliamentarians we should play our part in addressing the epidemic. At home in the UK, where around 77,000 people are infected with HIV, we believe that careful policy, respectful of human rights, is critical to tackling the disease and the serious social exclusion that can go along with it. Abroad, where HIV infection rates run as high as 26% and people die every day, we believe we have a responsibility to help.

There are over 200 members of the APPG on AIDS and the views presented in this report are not necessarily shared by every member.

The Treatment Timebomb

Report of the Enquiry of The All Party Parliamentary Group on AIDS into long-term access to HIV medicines in the developing world

Introduction

The UK Government, along with other signatories to the Millennium Development Goals, has signed up to achieving Universal Access to HIV prevention, treatment, care and support by 2010. This is a staging post for the longer term Millennium Development Goal to 'halt and reverse the spread of HIV/AIDS by 2015'.

We are not on track for either target. With less than a year to go before 2010, only a third of those who need HIV treatment have access to it. That is in itself a cause for urgent action. However, in our drive to achieve these targets, we must not forget that they do not represent the end of the HIV story. All those millions of people who do get on treatment will need to continue being treated, cared for and supported for many decades to come. The prevention programmes must also continue, because treating ever-growing numbers is unsustainable and only prevention can ensure the spread of HIV is reversed once and for all.

The need for a long-term vision has generated this enquiry which focuses on treatment. The APPG chose to address treatment because it is one of the areas that we in the north can influence and that those in the south have least control over. Northern companies and scientists develop the drugs, northern institutions regulate and approve them for human use, northern dominated trade rules affect who can access them and at what price, and – crucially - these rules determine whether or not a competitive market can develop. We have a responsibility to make the global rules, which we have created and continue to control, work in the interests of the poor.

This enquiry shows that we are sitting on a treatment timebomb. We can predict many of the changing treatment needs of people living with HIV in the coming decade and they are not compatible with treatments and prices available today. Maintaining HIV treatment to keep people alive will cripple developing economies, or place unbearable strains on richer countries trying to support them. Action is needed now, to avert crisis later.

The format of this report

Section One	Looks at the rising numbers of people who will need HIV treatment beyond 2015;
Section Two	Looks at the changing drugs that people need – and the cost implications;
Section Three	Analyses the factors that have reduced prices in the past;
Section Four	Considers whether these factors can be used again to reduce prices of newer drugs;
Section Five	Considers what new medicines/ formulations need to be developed for HIV and how the required research can be funded;
Section Six	Concludes the report.

Section One

The numbers of people needing treatment will rise dramatically beyond 2015

The numbers of people who need treatment for HIV is rising and will continue to rise for many years ahead. The reasons for this are given below.

Epidemiological projections beyond 2015 are being developed by UNAIDS, but early stage research into long-term Antiretroviral Therapy (ART) needs in Zimbabwe, for example, showed that even if all who need treatment have access to it by 2010, the numbers in need will be six times greater by 2030.¹ A crude scale up to a global level would indicate the global numbers in need of treatment will be in the region of 55 million people by 2030. Today we are treating less than four million; by any calculation the task ahead is enormous.

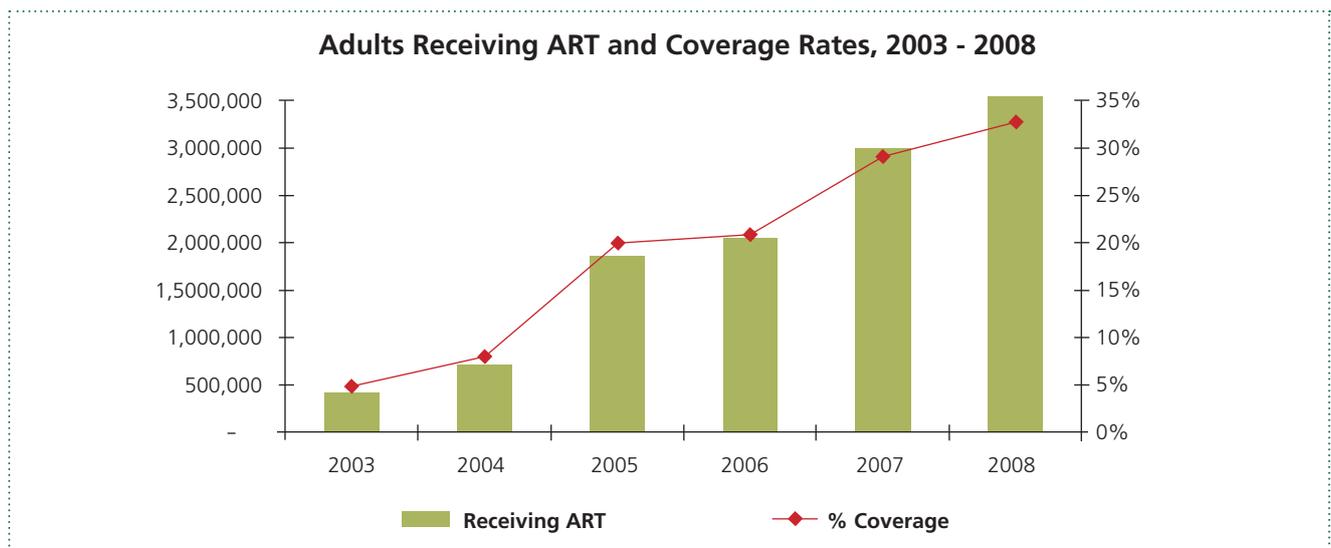
A consortium of partners called AIDS 2031, is currently working on a model that should be able to project a more precise figure for ART needs by 2031, by the end of this year. What is already clear is that in just a few years there will be several tens of millions of people who need HIV treatment.

Reason 1: Unmet need

Some of the projected rise reflects current unmet need – only one third of adults who need treatment are currently getting it.

The unmet treatment need amongst children is even worse with barely 10% of children in need currently accessing treatment, according to the UNAIDS 2008 Report on the Global AIDS Epidemic.² There will be increased demand for paediatric drugs – anti-retrovirals (ARVs) and Cotrimoxazole Preventive Therapy - especially when better medicines and formulations for children become available. The higher rates of children accessing treatment in some countries, such as those that the Clinton Foundation and PEPFAR work in, demonstrates that this scale up is possible with adequate resources and political will.

Figure 1



Source: Clinton Foundation HIV/AIDS Initiative, 'Paediatric Treatment Program 2008 Performance Report' March 2009

1 'Estimating the Resources Required in the Roll-Out of Universal Access to Antiretroviral Therapy in Zimbabwe' TB Hallett, S Gregson, S Dube1, ES Mapfeka, O Muguringi & GP Garnett

2 UNAIDS Report on the Global AIDS Epidemic 2008
http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp

The use of ARVs to prevent mother-to-child transmission also needs to be scaled up, with the latest figures showing only one third of mothers with HIV having access to the appropriate treatment.³

With no interventions, around one in three babies born to HIV positive mothers will be HIV positive.⁴ Some of these children are infected at birth and some through breast-feeding. Preventing mother to child transmission is relatively simple and must be a priority if we are to slow the HIV epidemic.

Finally, the majority of people in the world who are HIV positive don't know their HIV status. The roll-out of testing programmes and money invested in strengthening health systems should help identify these adults and children. In this case the extra demand for ART is a reflection of success.

In addition to the rise in number of people in need of ART, there will be an increase in demand for treatments for common co-infections. If left untreated, serious infections such as TB can accelerate the impact of HIV, leading to premature death. Any investment in ART therefore should go hand-in-hand with an investment in common serious co-infections or opportunistic infections.

Reason 2: People staying alive and needing treatment for longer

The total number of people living with HIV will rise, as people stay alive. They will all continue to need treatment. Again, this is a reflection of success. As health systems improve and the quality of care and support given to those living with HIV improves, lives will be extended.

Reason 3: People should be starting treatment earlier

The size of the rise in demand and expenditure on HIV treatment will reflect policy decisions and the availability of CD4 testing.

A key policy decision will be at what stage in their infection people should start receiving treatment.

A CD4 count measures the strength of a person's immune system, with 800-1500 cells per cubic millimetre of blood being a normal healthy count; and below 200 being a typical count for someone with AIDS symptoms. In developed countries, such as the UK, guidance is that when a patient's CD4 count drops to 350 they need to start treatment.⁵ The WHO international guidelines however, are that ART should start at 200, in the absence of specific symptoms. Many argue that this is leaving treatment too late and there is pressure on the WHO to update its guidelines. Recent research shows that initiating treatment at a CD4 count under 350 increases the risk of death by 69%.⁶

However, most developing countries are not even treating people at the WHO recommended level; the average starting point for anti-retroviral therapy in low income settings is even lower, at just above a CD4 count of 100.⁷ This is partly because the judgement about when to initiate therapy is being taken on the basis of symptoms rather than by a CD4 test result. Symptoms often do not start appearing until the CD4 count drops below 200, so it is not surprising that people diagnosed symptomatically are diagnosed late.

CD4 counts

800 - Or over is a healthy CD4 count

350 - Patients start HIV treatment in the UK

200 - WHO recommends HIV treatment should start, unless patients already have symptoms. Many argue this is too low and should be revised to 350 or more.

100 - The average count of people starting treatment in developing countries is just above this number. This is dangerously low and people will already be very ill.

3 UNICEF Children and AIDS Third Stocktaking report 2008

4 UNAIDS 'Rates of Mother-to-Child Transmissions and the Impact of Different PMTCT Regimens' 2005
<http://www.epidem.org/Publications/PMTCT%20report.pdf>

5 British HIV Association (BHIVA) guidelines

6 'Rationing Antiretroviral Therapy in Africa- Treating Too few, Too Late' N Engl J Med 2009; 360 (18): 1808-10 N Ford, E Mills & A Calmy. http://www.msfaaccess.org/fileadmin/user_upload/diseases/hiv-aids/hiv-2009/TreatingTooFewTooLate.pdf

7 'Rationing Antiretroviral Therapy in Africa- Treating Too few, Too Late' N Engl J Med 2009; 360(18): 1808-10 N Ford, E Mills & A Calmy.

CD4 test machines are expensive and require trained personnel to use them. There is no accurate data on the extent of the use of CD4 test machines in the developing world; although we know they are not the norm. A cheap, easy to use CD4 test is currently being developed by the CD4 Initiative, a public private partnership, which aims to have the test available in 2011.

Research has shown that whether anti-retroviral therapy is initiated on the basis of a symptomatic or CD4 diagnosis is one of the most significant factors in determining the long term need for ART, not only because people start treatment sooner but also because of the impact of early diagnosis on survival.⁸ Projections based on this research estimate that, while improving the effectiveness of treatment, moving to CD4-based rather than symptoms-based ART initiation could almost double ART needs over the period 2010 to 2030.

If national or WHO policies on eligibility for treatment change, or if CD4 tests rather than symptomatic diagnosis methods become the norm, a new cohort of people living with HIV, who otherwise would not have been considered eligible for treatment, will need to be treated.

Reason 4: Public Health Policy

The other policy decision that may have an impact is the use of HIV treatment as prevention.⁹ Successful HIV treatment lowers the level of virus in a person's body and makes them significantly less infectious. Some countries may decide to get as many infected people on treatment immediately, rather than waiting for a specific CD4 count or for symptoms to appear, in an attempt to reduce new infections. This of course, if successful, would reduce need for treatment later. However, such a policy has not been tried yet and might be difficult to implement in the case of those who are infected but have no HIV-related symptoms, because of the unpleasant side-effects of treatment.

Reason 5: New Infections

At the same time, there will continue to be new infections, although if our prevention efforts are successful, these should be at a reducing rate. Nonetheless, these people will need to be treated. It is crucial that new infections are minimised. Currently for every two people on treatment, five are newly infected.¹⁰

8 Estimating the Resources Required in the Roll-Out of Universal Access to Antiretroviral Therapy in Zimbabwe' TB Hallett, S Gregson, S Dube1, E.S. Mapfeka, O Muguringi & GP Garnett

9 Lancet 26th Nov 2008.

10 DFID HIV and AIDS In-depth 2009 <http://www.dfid.gov.uk/Global-Issues/How-we-fight-Poverty/HIV-and-AIDs/HIV-and-AIDs-in-depth/>

Summary

Reasons One to Four, reflect positive scenarios, where people live longer, are able to access the treatment they need and start treatment early enough to optimise their long-term health. They point to the need for long-term investment in treatment and in the care and support that needs to go with it.

The long term commitment that each new HIV infection calls for is a reminder of the importance of prevention. The cost of treating someone with HIV for life means it makes financial as well as ethical sense to minimise new infections. There is particular potential to do this by preventing mother-to-child transmission, where currently opportunities are being missed.

Universal Access to treatment is only possible in a context where there are health systems with appropriately trained staff, and so the implications of these projections go far beyond the simple cost of medicines. Nonetheless, given the numbers involved, it is important that the unit cost of medicines is kept as low as possible and that competitive markets and economies of scale are used to effect. An increasing medicines bill will place undue burden on the health service and risks detracting money from other areas. However, as the next section shows, the cost of treating people is likely to rise.

Recommendations

1. HIV needs to be understood as both an emergency for those without treatment and as chronic condition for those with it. Developed and developing country governments and donors therefore need to make long term plans, beyond 2015 for funding and deploying an adequate response.
2. Key organisations purchasing HIV medicines, such as the Global Fund, UNITAID and PEPFAR, require assurances from donors that financial commitments will be secured for the longer term.
3. Advocates of universal access to HIV treatment, care and support need to agree on a common message to drive and maintain progress beyond 2015.
4. Treatment is needed to save lives, but prevention is the only way to manage the epidemic in the long term. Each infection averted saves years of treatment costs. Developing country governments, international NGOs, donors and others should work together urgently to develop best practice recommendations on prevention:treatment spending ratios.
5. UNAIDS should collect data on the extent of the use of CD4 tests, and donors should stand ready to fund the roll-out of a cheap, easy to use CD4 test as it becomes available. This could dramatically improve survival rates for people with HIV.

Section 2:

The drugs that people need are changing; and they're more expensive

The number of people needing HIV treatment will rise over the next two decades and so will the cost of treatment. This is because better, more effective treatments have come on the market and should be offered to patients, and also because, over time, more people will move from first to second (and later) line regimens, which are more expensive. These factors are explained below.

Factor 1: High price of tolerable first line HIV medicines

The majority of people living with HIV in the developing world are treated with a combination of three drugs: Lamivudine (3TC), Stavudine (d4T) and Nevirapine (NVP).¹¹ Stavudine has a common side effect of lipodystrophy – the effects of which include changes in weight, with fat loss in the limbs and face and fat gain around the stomach, shoulders and neck – these effects are shown in the photo below. The symptoms can remain long after its use has ended. In addition to this, it is highly toxic and can cause life threatening lactic acidosis and so is rarely used in high income countries. Whilst some people are able to tolerate it, others react badly, and this can also have an affect on adherence. In one of Medecins Sans Frontieres' AIDS projects in Rwanda, almost one in every six people on Stavudine had to change their regimen due to toxicity.¹²

In 2006, the WHO recommended that treatment providers move to less-toxic regimens, based on either Zidovudine (AZT) or Tenofovir (TDF). The Clinton HIV/AIDS Initiative projects that first line antiretroviral (ARV) demand will continue to shift progressively away from Stavudine-based regimens towards these clinically superior but more expensive regimens.¹³



However the price of these superior drugs has meant progress has been slow. Currently the Tenofovir-based combination costs at best \$210¹⁴ per patient per year compared to \$87¹⁵ per patient per year for the basic Stavudine combination. In countries where the originator companies have patents, the Tenofovir combination is even more expensive at up to eleven times the price of the Stavudine-based combination.¹⁶

The girl in this photo is eight years old. She lives in South Africa. She has severe lipodystrophy, having been on a Stavudine-based (d4T) based regimen. The symptoms have persisted since ending the Stavudine-based treatment 4 years ago. Printed with permission from www.righttocare.org

11 WHO 'Towards Universal Access – Scaling up priority HIV/AIDS interventions in the health sector' 2008. WHO/UNAIDS/UNICEF, June 2008 shows 51% of patients in 30 low and middle income countries are on this combination. The next most popular combination is used by just 14%

12 MSF 'UTW: Interview with Campaign Pharmacist' <http://www.msfastcess.org/main/hiv-aids/utw-interview-with-campaign-pharmacist/>

13 CHAI written evidence to the APPG on AIDS

14 As reported, Reuters UK 'Generic Deal Cuts Cost of AIDS Drugs Further' April 17th 2009 <http://uk.reuters.com/article/healthNews/idUKTRE53G00O20090417?rpc=401&>

15 MSF 'UTW: Interview with Campaign Pharmacist' July 2008 <http://www.msfastcess.org/main/hiv-aids/utw-interview-with-campaign-pharmacist/>

16 MSF 'UTW: Interview with Campaign Pharmacist' <http://www.msfastcess.org/main/hiv-aids/utw-interview-with-campaign-pharmacist/>

Factor 2: Better drugs are needed for preventing mother-to-child transmission

In 2007, 49% of women living with HIV in low and middle income countries received a single dose of Nevirapine during pregnancy to prevent transmission of HIV to their babies during birth.¹⁷

Nevirapine is cheap at around five US cents per dose and simple to use, however there are serious drawbacks to this option for both mother and child. The drug is not as effective as alternatives; assuming a mother breastfeeds for only six months, it reduces the chance of transmission by about half to 16%, but does not eliminate it¹⁸. Where mothers are breast-feeding for longer, even more children are likely to be infected. Single dose Nevirapine may also cause resistance to subsequent treatment involving Nevirapine and Efavirenz, reducing a mother's subsequent treatment options and those of her child, and creating the need for them to use more expensive treatment regimens.

According to WHO guidelines, the regimen currently recommended for preventing mother-to-child transmission in resource-limited settings uses a combination of Zidovudine from six months gestation, a single dose of Nevirapine at birth and a week of Zidovudine and Lamivudine after delivery. This approach is more difficult to administer than single dose of Nevirapine, but it is also significantly more effective, with ten percent of babies infected at six months, assuming they too are breastfed.¹⁹ This combination is also less likely to lead to drug resistance.²⁰

The difference in cost of the two options is significant, with single dose Nevirapine costing only less than a dollar and involving little medical time compared to around \$24 for the Zidovudine option, which involves medicines taken twice daily for 12 weeks.

Putting HIV mothers on full anti-retroviral therapy is more expensive and involves a more sophisticated diagnostic work-up, but is the most effective method for transmission prevention. Given that HIV positive mothers will in any case need treatment for their own health either immediately or when their CD4 count has dropped further; saving money by delaying their treatment for a few months, whilst risking the health of their baby, does not seem a sensible choice.



In the developed world triple combination therapy, combined with the use of caesarean section and a 'no breastfeeding policy' is achieving transmission rates of under 1% but the costs of this comprehensive approach are prohibitive in the developing world.

A note on breastfeeding

The transmission figures cited above assume breastfeeding because of the high number of women in least developed countries who do not have access to clean water and/or cannot afford to buy infant formula milk. Mixing formula with dirty water is very dangerous for a baby, particularly if they have not had the benefit from protective anti-bodies in their mother's milk. However, breastfeeding by an HIV positive mother for six months increases risk of transmission to the child by a further 10% of the original risk.²¹ So women are faced with very difficult decisions. Clearly therefore clear breastfeeding policies, availability of clean water and affordability of formula milk could also significantly improve mother-to-child transmission rates.

Photo: This little Zambian girl has been orphaned by AIDS. Her mother didn't get the treatment she needed to keep her alive, or the treatment she needed to prevent her passing on the infection to her daughter, who is now very ill. She is being looked after by her grandmother, who is pictured here.

17 UNICEF Children and AIDS Third Stocktaking report 2008

18 ibid

19 ibid

20 AVERT: HIV and AIDS 'Preventing Mother-to-Child Transmission of HIV'
<http://www.avert.org/motherchild.htm>

21 UNAIDS 'Rates of Mother-to-Child Transmissions and the Impact of Different PMTCT Regimens' 2005 <http://www.epidem.org/Publications/PMTCT%20report.pdf>

Factor 3: The high price of second line and subsequent medicines

As a virus, HIV constantly mutates in the human body and becomes resistant to the medication taken. The development of resistance is likely to happen to everybody over time, but the process is accelerated when patients fail to adhere to their regimen, which happens more frequently in resource poor settings often due to treatment stock outs. Once the first set of medicines (first line) stop working, moving on to second line medicines is a matter of life or death.

The cheapest price for a second line regimen is \$590²² per patient per year; this makes it seven times more expensive than the cheapest first line drugs. Furthermore, where the same drugs are patented by originator companies and generic purchase is not possible, prices are up to seventeen times the price of first line drugs.²³

Most second line medicines are more complex than first line ones. The protease inhibitors used in second line regimens are typically bigger and more complex than first line drugs at a molecular level. A number of second line drugs are also dosed at higher levels, requiring more active ingredient per day of treatment. This means that they may never be quite as cheap as the first line medicines; however there are some opportunities for price reductions.

Currently only 3% of those receiving ARVs are being treated with second line drugs in developing countries but this is projected to rise to 5% by 2011, to a total of around 260,000 people.²⁴ Several international organisations have developed their own calculations for second line migration; the Global Fund to Fight AIDS, TB and Malaria, for example, works on the basis of 5% migration from first to second line medicines per year²⁵. In Medecins Sans Frontieres' longest-running AIDS project in Khayelitsha, South Africa, approximately 22% of patients on treatment for five years needed to be switched to a second line drug combination.²⁶

Ultimately there will also be a need for third and fourth line drugs for people who have already been on treatment a long time and developed resistance. These are even more expensive, and not readily available.

When to switch?

In high income countries, decisions about when to move a patient from first to second line treatment or subsequent treatments are usually taken on the basis of a viral load test. This shows how successfully a treatment regime is in suppressing the virus in the body. However, these are expensive and require trained staff and therefore are not commonly used in developing countries. As a result, it is likely that demand for second line drugs will be slower than is clinically called for. This not only damages the individual's health, it creates a risk that he or she will transmit a resistant strain of the virus to other people.

The current price of viral load tests means that their use is probably a less effective use of resources than extending ART to new people who need it.²⁷ Nonetheless, investment in the prevention of resistance to first line drugs will generate savings in the medium term and therefore the development of cheaper, and ideally point-of-care, viral load tests should be one of the research and development (R&D) outcomes HIV research funders seek to achieve.

22 As reported, Reuters UK 'Generic Deal Cuts Costs of AIDS Drugs Further' April 17th 2009 <http://uk.reuters.com/article/healthNews/idUKTRE53G00O20090417?rpc=401&> This price already reflects the work of UNITAID and Clinton Foundation to buy in bulk.

23 MSF 'UTW: Interview with Campaign Pharmacist' <http://www.msfacecess.org/main/hiv-aids/utw-interview-with-campaign-pharmacist/>

24 Figures from Clinton Foundations ARV Market Update January 2009 for the number of people on 2nd line treatment in 'generic accessible' markets.

25 Verbal evidence from the GFATM, APPG visit to Geneva.

26 MSF 'Untangling the Web of Anti-retroviral Price Reductions', 11th edition July 2008

27 'Outcomes from monitoring of patients on antiretroviral therapy in resource-limited settings with viral load, CD4 cell count, or clinical observation alone: a computer simulation model' Lancet 2008; 371: 1443–51. A N Phillips, D Pillay, A H Miners, D Bennett, C F Gilk &, J D Lundgren

Efforts to prevent resistance by supporting patients to adhere to their regimens are an important way of delaying the need for second line treatment. Fixed dose combinations - which are several medicines in one pill - would also help patients to comply with treatment, as would better labelling. The need for new fixed dose combinations is considered later in this report. Counterfeit medicines (medicines that have not been approved by a regulatory authority and are produced illegally) are also likely to contribute to resistance and developing countries need support to tackle criminals involved in supplying them. Investment in such measures should deliver long-term savings as resistance and the need for second line and subsequent regimens is reduced.

Factor 4: Price of related medicines and diagnostics

When considering the cost of treating a patient with HIV, it makes sense also to consider the cost of treating any likely symptoms. There is a need to address the price of drugs and diagnostics to diagnose and treat opportunistic infections associated with HIV, such as TB diagnostics, second line TB drugs, Hepatitis C medicines, antibiotics for infections such as pneumonia, and treatments for many other conditions. A full analysis of the costs of these treatments and opportunities for cost reductions cannot be done here but would be a useful piece of research.

Summary

Many ARVs have adverse effects, and affordable, improved first line drugs are needed urgently. There must also be a move towards more affordable effective regimens for preventing mother-to-child transmission and this should be a priority. The price of second line and subsequent treatments must also be reduced before large numbers of people need them.

Recommendations

1. Donors and developing countries should invest in the use of more effective PMTCT (prevention of mother-to-child transmission) drugs, as this will save money in future and lives.
2. Urgent action needs to be taken to reduce the cost of the WHO recommended first line alternative to the basic d4T+3TC+NVP combination, to enable the treatment of those who cannot tolerate Stavudine.
3. Urgent action needs to be taken to reduce the cost of second line medicines, which are a matter of life and death to those who need them.
4. There is a need for research into the costs of treating common opportunistic infections so that realistic financial allocations can be made when planning HIV programmes.

Section 3:

Drivers of anti-retroviral medicine price reductions in the past

The most basic HIV drugs are now sold to low income countries at less than one percent of their original cost. In its enquiry, the APPG gathered evidence about how these price cuts were achieved and whether these factors would be applicable to the newer, more expensive drugs.

In May 2000 it cost just over USD \$10,000 to treat someone with HIV on the most basic first line combination, Lamivudine (3TC), Stavudine (d4T) and Nevirapine (NVP), for a year. This was the lowest world price. Today, the same drugs can be bought in low income countries for just USD \$87. The vast majority of that fall happened in just three months (see Figure 2). It is commonly agreed that these drugs, which are today's most widely used combination of ARVs, are almost at the lowest achievable level.

As the graph suggests, the most important factor in reducing prices has been generic production. When generic companies entered the market in 2000 offering much lower prices, the branded companies had to follow. Generic production was possible because patents were never granted or were invalid in the country of manufacture (India and Brazil) and there were no patent barriers in the importing country. This enabled multiple generic manufacturers to produce and sell the drugs, as well as the innovator companies. Competition increases incentives for suppliers to find ways of driving cost reductions. Figure Two shows the dramatic price effect of the entry of generic suppliers into the ARV market.

Figure 2: The impact of generic competition on the price of basic triple combination therapy: d4T (stavudine) + 3TC (lamivudine) + NVP (nevirapine).

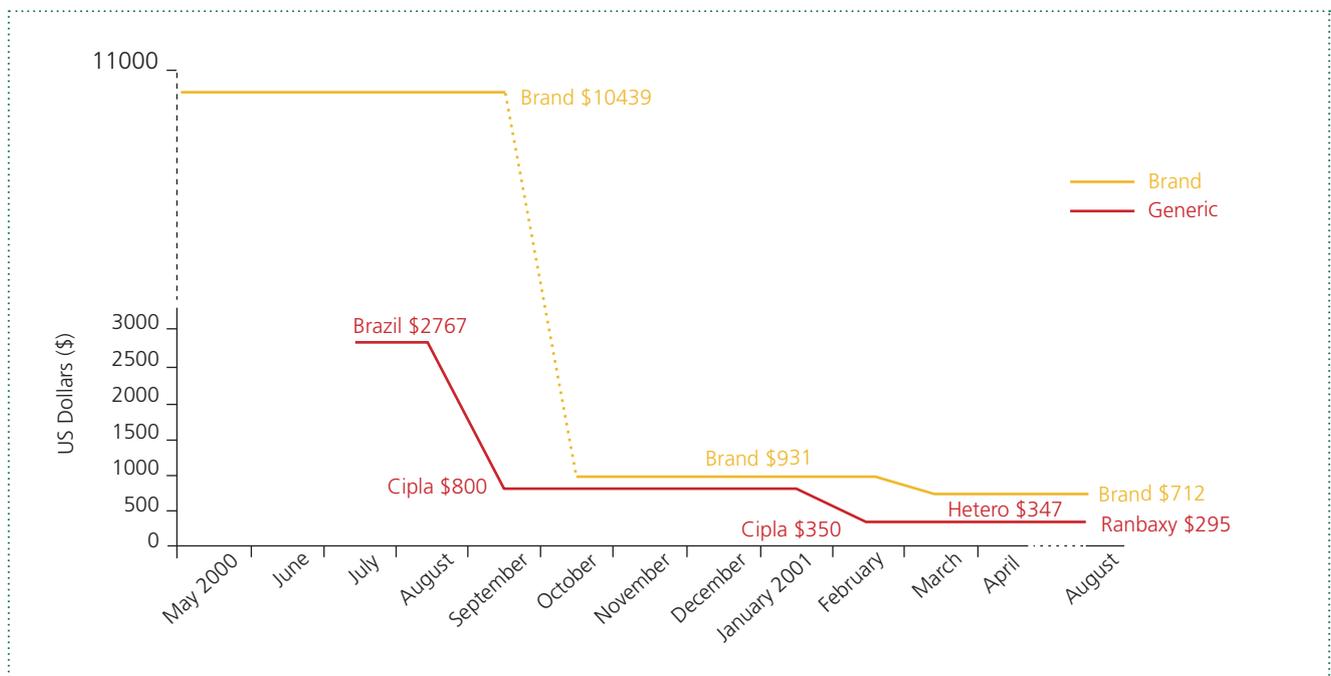


Figure 2 shows the lowest world price per patient per year at each time point. It is reprinted with permission from Avert: www.avert.org. Since August 2001 lowest prices for this combination have dropped still further to \$87 USD.

Other factors affecting price

The majority of the price difference between today's triple combination and the same combination in May 2000 occurred before 2002 with the entry of new generic manufacturers onto the market. However, there have been other developments that have reduced prices. These are:

Volume and predictability

The volume of HIV medicines purchased by the Global Fund for AIDS, TB and Malaria and PEPFAR have massively increased the market for these drugs in the last five years and this has helped achieve economies of scale. For medicines that have already come down a great deal in price, such as the basic Lamivudine (3TC), Stavudine (d4T) and Nevirapine (NVP) combination, increased volume has been an important factor bringing prices to their lowest yet. As the Clinton HIV/AIDS Initiative said in their evidence:

"Perhaps the single biggest driver in manufacturing costs is volume, which enables manufacturers to achieve efficiencies of scale, spread fixed costs, and negotiate volume discounts on raw materials. Consequently, any intervention to scale up treatment programs is also inherently an intervention to lower manufacturing costs and prices. "

UNITAID has played an important role in facilitating price reductions for HIV/AIDS drugs through bulk purchase agreements.²⁸ It has also helped to coordinate more predictable ARV market demand, although there is room for improvement on this. Both Gilead and GlaxoSmithKline raised the need for improved demand forecasting in their evidence to the APPG.

UNITAID

UNITAID was founded in 2006 by Brazil, Chile, France, Norway and the United Kingdom; since then membership has grown to 27 States, including many developing countries. Its mission is to "contribute to the scale up of access to treatment for HIV/AIDS, malaria and tuberculosis in low and middle income countries by leveraging quality drugs and diagnostics price reductions and accelerating the pace at which they are made available."

Hosted by the WHO in Geneva, UNITAID does not have its own programmes for the distribution of medicines but supports programmes by its partner organisations such as The Global Fund and the Clinton Foundation. It has already had considerable success in lowering the price of medicines through negotiated bulk purchases and by other means. It is currently working on developing a patent pool (described later in this document). *The APPG visited UNITAID as part of its enquiry.*

Pharmaceutical company access programmes

All the major originator companies have some sort of programme to improve access to their HIV medicines in the developing world. UNAIDS has been responsible for persuading many companies to establish such schemes. Different companies take different approaches. Whilst some (such as Abbott) provide their own medicines via a tiered pricing system for developed, middle income and developing countries, others (such as Gilead) grant generic companies voluntary licences to produce their medicines. Schemes are established drug by drug, so also differ within companies.

²⁸ As reported, Reuters UK 'Generic Deal Cuts Costs of AIDS Drugs Further' 2009 <http://uk.reuters.com/article/healthNews/idUKTRE53G00O20090417?rpc=401&>

Of the models, voluntary licences when issued to a significant number of generic manufacturers seem to be best at reducing prices. However, there has been no independent thorough analysis comparing the relative costs and benefits of the many models available in terms of their impact on access, the time taken to reach developing country markets, and the cost to the originator company. An independent analysis would provide useful knowledge to improve access programmes.

A common problem with tiered pricing is that the medicines are not registered for use in many developing countries, so while in principle a price may be available, in practice neither the price, nor the medicine itself is available.²⁹ This is often because the lengthy and cumbersome process of registering a drug in every country makes companies reluctant to register new drugs in developing countries, especially where there is a limited commercial market. In other cases the registration process has started but is taking months or years to complete. Support for developing countries to improve their registration process would help make tiered pricing a more effective approach. DFID should be encouraged to continue its work on this.

Evidence from the Treatment Action Campaign in South Africa, called for better monitoring of access programmes to ensure that promises of cut-price medicines in tiered pricing systems were actually delivered. They argued that there was currently minimal accountability to the countries and patient groups for whom such medicines are intended. If companies were willing to regularly open up their access programmes to an independent auditor, and publish the results, this might increase the confidence of some of the grass-roots organisations in them. It would also benefit the image of pharmaceutical companies more broadly, including in developed countries, and a successful audit could be a badge of Corporate Social Responsibility quality.

Summary

In conclusion, generic competition has been central in reducing the price of ARVs, but other factors that have helped reduce prices have been volume, a predictable and organised market that can pay its suppliers promptly, and pharmaceutical access programmes. The next section will consider whether these same factors can be used to reduce the price of the newer HIV medicines that will become increasingly important in the years to come.

Recommendations

1. There should be an independent analysis of the relative costs and benefits of different types of pharmaceutical access programmes. DFID would be well-placed to conduct this.
2. Pharmaceutical companies should open up their access programmes to independent audit to increase confidence in them.
3. Buyers of ARVs should continue to work together, with the support of the WHO, to provide reliable forecasts to the pharmaceutical industry of the volumes they intend to procure.

Section 4:

Opportunities for reducing the cost of new HIV medicines

DFID indicated in its AIDS strategy, launched in 2008, that it believes there is scope for £50 million of efficiency savings in the purchase of ARVs and pointed to the important impact this could have on access to medicines saying “Reducing the costs of drugs could enable savings that could fund access to life-saving treatment for an additional one million people every year, even without new resources. The UK will work with others to help make this happen.”³⁰

Since in the past generic competition appears to have been the most significant factor in reducing the prices charged for HIV drugs, this section, Part A, considers it separately, with its own recommendations before considering other factors which might reduce prices in Part B.

Part A: Generic production

Most of the newer expensive drugs are currently being produced under patent, which prevents wide generic manufacture and keeps prices high. The status of the patents on specific drugs varies from country to country.

The legal environment surrounding patents has tightened since the most commonly-used and cheapest ARVs were first produced by generic manufacturers. This is as a result of the implementation of World Trade Organisation (WTO) rules adopted as part of the Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement. There is a full explanation of TRIPS on page 21.

India, where the vast majority of generics are developed and produced, made its patent law compliant with the TRIPS agreement in 2005. Prior to this, it was much easier for companies to manufacture generic versions of HIV medicines. For example before TRIPS were introduced, the law did not allow products to be patented, only processes. If a generic company could invent an alternative process for manufacturing a particular product there was no patent infringement. This process, known as ‘reverse engineering’, was pioneered and perfected by Indian companies during the 1970s and 1980s.

However more recently, in preparation for 2005 and subsequently, patent laws have tightened and companies have had to change their behaviour. This is particularly significant for drugs invented after 2005, as product patents prohibit the entry of generic manufacturers into the market for the newer drugs. The drugs affected include important first line therapies recommended by the WHO.

Least developed countries (India does not fit into this category), have until 2016 to implement TRIPS.

Over-riding patents for public health purposes

Countries are legally allowed to overcome patent barriers for public health purposes by using TRIPS flexibilities (described in the TRIPS text box on page 21) in order to either produce their own generic versions of HIV drugs or import them. However these flexibilities have proved very difficult to make use of in practice. Respondents to the APPG enquiry described the lack of capacity and legal know-how of developing countries to exercise the flexibilities; and the impenetrable paperwork required.³¹ Heavy political pressure from companies and foreign governments (including the UK in its role in the EC) not to use the flexibilities was also cited as a common problem.

Despite all the barriers to their use, some countries have been able to issue the ‘compulsory licences’ which enable the generic manufacture of drugs under patent. Thailand for example issued a compulsory licence in January 2007 for the important drug Ritonavir, reducing its price significantly.

30 As reported, Reuters UK ‘Generic Deal Cuts Costs of AIDS Drugs Further’ 2009 <http://uk.reuters.com/article/healthNews/idUKTRE53G00O20090417?rpc=401&>

31 MSF ‘Untangling the Web of Anti-retroviral Price Reductions’, July 2008.

Unsurprisingly, the evidence to the APPG on the issue of use of TRIPS flexibilities differed widely between the pharmaceutical companies, who were in favour of a very restrictive use, and charities, who were in favour of more frequent use. The Doha Declaration which clarifies TRIPS does make it clear that “Each Member [country] has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.”³²

Medecins Sans Frontieres argues in its 2008 report ‘Untangling the Web of Anti-retroviral Price Reductions’ that “Tomorrow’s battle for access to affordable ARVs will need to be fought in a different way. It will require routine use of public health safeguards in patent laws, and of flexibilities in the World Trade Organization’s TRIPS Agreement, such as compulsory licensing. Increased global patenting through TRIPS is systematically reducing possibilities of producing generics, thereby changing the rules of the game and keeping prices high for the newer medicines people need. This puts a serious strain on, and threatens the sustainability of, national AIDS treatment programmes that are already struggling to implement and scale-up treatment.”³³

Helping countries to make the most of their patent flexibilities

Developing countries can get technical assistance with using TRIPS flexibilities from the World Intellectual Property Organisation (WIPO). However, WIPO is mainly funded by industry and it has been criticised for providing assistance which takes insufficient account of the role TRIPS flexibilities could play in promoting access to medicines.³⁴ This may change because, following pressure from member states WIPO has started to work on a development agenda. WIPO proposals in 2007 included:

“WIPO technical assistance shall be, inter alia, development-oriented, demand-driven and transparent, taking into account the priorities and the special needs of developing countries, especially Least Developed Countries...”³⁵

In practice, it may take some time to embed this development agenda within the organisation.³⁶ Other sources of technical support do exist and Germany in particular is driving forward this agenda, but funding for this is limited. These sources of support include United Nations Conference on Trade and Development (UNCTAD), InWent (a German organisation providing training courses on TRIPS flexibilities) and GTZ among others. The WHO also has a key role in providing assistance and monitoring the effect of new laws on access to medicines.³⁷

Regional cooperation is also useful in negotiating the use of TRIPS flexibilities. The International Community of Women Living with HIV (ICW) drew attention to the potential of regional cooperation to form bargaining blocks on intellectual property issues in its evidence. ICW cited examples of this being done successfully in Latin America with ten countries getting together to reduce the price of ARVs and HIV diagnostic tests with agreements from both originator and generic manufacturers.

New challenges to use of patent flexibilities

As described in the TRIPS text box (page 21) some countries are being put under pressure to go beyond the patent protection required in TRIPS, this is known as TRIPS+. TRIPS+ measures are often agreed as part of wider economic negotiations. Some countries, for example, have traded in their right to patent flexibilities in return for other economic benefits. The EC has been an important instigator of such negotiations.

32 Adopted 14th Nov 2001, Clause 5b, Declaration On The Trips Agreement And Public Health, WTO.

33 MSF ‘Untangling the Web of Anti-retroviral Price Reductions’, July 2008

34 Verbal evidence from the International Centre for Trade and Sustainable Development (ICTSD), APPG visit to Geneva

35 WIPO, “The 45 Adopted recommendations Under the WIPO Development Agenda”, 2007, <http://www.wipo.int/ip-development/en/agenda/recommendations.html>

36 Verbal evidence to the enquiry from the ICTSD

37 The WHA Resolution 61.1 adopted at the WHA 2008, which covers the Global strategy and a part of the plan of action on Public Health, Innovation and Intellectual Property, requests WHO to provide technical support, upon request, to Member States intending to make use of TRIPS flexibilities to promote access to medicines

Current negotiations between Costa Rica and Andean nations and the EC include provisions for 'test data protection' for a period of 10 years after drug approval. 'Test data protection' means that any generic company wanting to produce a medicine has to provide their own data showing its safety and efficacy. Without this measure, all that is required is proof of bio-equivalency to the original drug, which is a much cheaper and more simple process.

A second worrying development is the repeated detention of medicines, including HIV medicines, in European ports as they are in transit from a manufacturing country to a developing country. The medicines are being detained on the basis that they violate European patent laws in a bid to combat the trade in patent-infringing goods; however they are not intended for the European market, but for countries where there is no such patent. The ability of generic manufacturers to transport their goods is central to delivering medicines to millions of people with HIV in the developing world. Even temporary detentions/impoundments can be very serious, as they can lead to medicine stock-outs, leading to treatment interruptions, potentially causing people living with HIV to develop resistance to their medicines.

Least developed countries' TRIPS grace period

Least developed countries do not have to be TRIPS compliant until 2016. Many respondents (including Oxfam and HAI Africa) to the APPG enquiry cited the importance of the use of this period to establish production of generic medicines. This is already happening to some extent with interesting partnerships being created to share knowledge and develop the capacity of least developed countries to manufacture their own medicines.

Cipla, the Indian generic manufacturer, has entered into a partnership with a Ugandan firm to set up a factory making HIV and malaria drugs in Uganda. Cipla supplies the expertise and is training Ugandan technicians. The Ugandan government has pledged to procure ARVs worth \$45 million per year for seven years. The factory started producing in February 2009. They predict they will be producing ARVs at a cost of \$9 per month per patient and that they will be manufacturing two million tablets per day, these are only intended for the Ugandan national market. It is hoped that this will help Uganda's long-term ability to respond to its own HIV crisis.

Voluntary Licensing, Patent Waivers and Patent Pools

A final method of reducing the impact of patents on price is for the originator company to choose to waive them by issuing voluntary licences or non-assert declarations to certain manufacturers. The pharmaceutical companies Gilead and Boehringer are examples of companies that have done this for some of their medicines. Originator companies can also charge a royalty on the production of their medicines through a voluntary licence, which makes the scheme more sustainable for them. Voluntary licences on fair terms can also represent an effective way to avoid expensive and damaging legal battles over compulsory licensing.

The impact of these voluntary partnerships on price depends on the scope of the licence – where very few generic manufacturers are allowed to produce a medicine, the impact will be limited because competition is limited. Some licences also include conditions such as the requirement to buy the active ingredients from the originator company, which also limits their potential to reduce prices.³⁸

Gilead's Tenofovir is a good example of a voluntary licence that is having a positive impact on prices; this is because licences have been granted to eleven different generic manufacturers (all in India) who are competing with each other to supply the medicine at the cheapest rate. UNITAID are now purchasing generic versions of Tenofovir produced in this way. However Tenofovir, an important new first line drug, remains significantly more expensive than its older alternatives.

A broader form of voluntary licensing that is currently being proposed by UNITAID is a patent pool, where originator companies voluntarily put their patents (in this case ARV patents) into a single pool in return for a royalty. Manufacturers or researchers who wish to use the relevant patents are then able to do so for a fee. This has the advantage of creating a much larger field of competition, coming closer to a free-market whilst still preserving benefits for originator companies. The patent pool is discussed in greater depth in the research and development section of this document because it is also designed to facilitate the development of medicines better adapted for use in the developing world.

Summary (Part A)

Patent laws in India, the key generic ARV manufacturing country, have changed. The dramatic price reductions that were achieved around the year 2000 through generic competition are unlikely to be possible with the newer drugs. As more people become resistant to (or unable to tolerate) the cheapest older drugs, we are facing a treatment timebomb.

In the short term there is scope for generic production in some of the least developed countries such as Uganda. By 2016 all member countries of the WTO will be TRIPS-compliant and the manufacture of generic versions of new drugs will be almost impossible. Before then, the international community must find new ways to improve competition in the ARV market that are palatable to pharmaceutical companies, because twenty-year global monopolies on the manufacture of life-saving drugs are not compatible with public health in the developing world.

Recommendations on enabling generic production:

1. WIPO should be held accountable to its development agenda, and asked to demonstrate examples of supporting developing countries to use their TRIPS flexibilities to protect public health.
2. DFID should consider supporting developing countries in their use of TRIPS flexibilities, both by funding technical advice and at a diplomatic and advocacy level, by encouraging cooperation from pharmaceutical companies.
3. Private partnerships between originator companies and generics can be profitable for all involved and improve access. Gilead's partnerships in India are an example of this. This approach should be encouraged.
4. Regional entities such as the East African Community (EAC), and its southern African equivalent the Southern African Development Community (SADC), that allow for cooperation among a group of countries, should work together to negotiate flexibilities and share lessons.
5. The UK Government should use its influence at the EC, particularly given the EC Trade Commissioner post is held by the British, to halt the adoption of TRIPS+ clauses in trade agreements that limit the ability of developing country governments to protect public health.
6. Customs authorities in EU states should desist from detaining life-saving drugs in their ports when these shipments are destined for third countries where no patent is infringed.
7. The UK Government should use its influence at the EU, to require a review of EU customs regulations that allow such detentions, and assess their impact on access to medicines.

What is TRIPS?

The Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement aims to lay down minimum standards for the way Intellectual Property is protected around the world. The World Trade Organization (WTO) administers TRIPS through the TRIPS Council, which consists of all WTO members. Disputes between countries concerning adherence to TRIPS may be taken to the WTO system for settlement. Developed, developing and least developed countries were given 1, 5 and 11 years respectively to comply with TRIPS.

What are the implications of TRIPS?

TRIPS set out a minimum level of patent protection of 20 years, during which generic companies are prevented from entering the pharmaceutical market and selling medicines more cheaply. The majority of the ARVs used in the developing world are manufactured by generic companies based in India, like Cipla. But India was obliged under TRIPS to introduce a TRIPS-compliant patent law by 2005. India's new patent law still restricts patentability of pharmaceuticals more rigorously than in developed countries. Nevertheless, the changes since 2005 seriously threaten its ability to produce generic versions of new medicines for use in the developing world.

TRIPS Flexibilities

The Doha Declaration in 2001 confirmed the legality of important flexibilities in TRIPS that allow countries to manufacture or import generic drugs. Where there is a public health imperative, countries can issue a compulsory licence to a generic manufacturer, on payment of a royalty to the owner of the patent. However, many of the countries with a high HIV burden are the least able technologically to set up their own manufacturing capacity, and meet the stringent regulatory requirement to produce high quality drugs.

However, the Declaration also led to an amendment to TRIPS which permits countries without manufacturing capacity to import under a compulsory licence from another country which has that capacity. Although yet to be ratified, the amendment has been in force since 2003 under a waiver to TRIPS. Even so, only one country (Rwanda) has utilised this facility.

Some respondents to the APPG enquiry cited heavy political pressure by pharmaceutical companies and developed country governments as an important barrier to the use of TRIPS flexibilities (Oxfam and Stop AIDS Campaign).

"We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health....we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all." Paragraph 4 of the WTO Doha Declaration

TRIPS+

Some developing and middle income country governments are giving up some of the flexibilities they have and even agreeing to more stringent patent protection rules (known as TRIPS+) in bilateral trade agreements. The TRIPS+ measure that, according to the Centre for International Trade and Sustainable Development (ICTSD), has the worst impact and represents about 90% of the medicine cost increases predicted, is the introduction of data exclusivity for pharmaceutical products. This means that companies seeking to produce generic versions cannot rely on clinical test data generated by the originator for a period of up to ten years, and would have to repeat such studies at considerable expense to bring a product to market. In its absence, they would only have to do relatively cheap tests for bioequivalence to demonstrate that their product has essentially the same bio-pharmaceutical properties as the original. This can delay the entry of generic manufacturers into the market by many years. In Costa Rica for example, ICTSD predict that TRIPS+ in the US-Central American Free Trade Agreement could lead to a price increase in absolute terms of 17% to 31% for all drugs over the covered active ingredients by 2030.

Part B: Other potential levers for reducing the price of HIV medicines

Volume and inclusion on Government procurement lists

Developing countries and pharmaceutical companies are in a ‘chicken and egg’ scenario, whereby countries do not feel able to put more expensive WHO recommended drugs, like a Tenofovir based first line therapy, on their list of drugs for governmental procurement and the companies therefore cannot manufacture them at sufficient volume to bring the price down. However, if this deadlock is broken there is significant opportunity for economies of scale, especially in the cost of active ingredients.

Consolidation around WHO recommended regimens

If countries were to consolidate their purchasing to a smaller number of standard regimens, for example those recommended by the WHO, this could increase the volume of key HIV medicine bought, facilitating economies of scale.

Barriers to such consolidation identified by respondents to the APPG enquiry were not only the price of the WHO preferred medicines (the chicken and egg scenario), but also poor communication about the benefits of new regimens. At the international level WHO needs to do more to publicise their guidelines and at a national level governments need to disseminate that knowledge not just to their capitals but to rural health centres.³⁹ Faith-based organisations and local NGOs can help by stimulating grassroots demand for better drugs.

However, respondents were keen to point out that WHO recommendations should not be followed blindly. For example, both Boehringer and the Clinton HIV/AIDS Initiative said that WHO needed to update its guidelines more frequently in relation to children’s HIV medicines.⁴⁰

The lack of relevant clinical data about the effectiveness of new regimens for developing country populations, and sub-groups, such as pregnant women, is also a barrier to the adoption of new regimens. At the APPG Roundtable, Professor Diana Gibb from the Medical Research Council highlighted the importance of local clinical trials to determine what is best for a particular country context.⁴¹ There is an urgent need for funding for such trials, which could make the WHO recommendations more relevant.

Professor Gibb also suggested that along with improved clinical data an equivalent of the UK’s National Institute for Clinical Excellence (NICE) would be useful for developing countries to gather evidence to make public health decisions about the costs and benefits of providing certain medicines. The WHO was supportive of this idea in interviews with the APPG.

Streamlining drug registration

Applying for drug registration in developing countries can be a slow process that adds to the cost of bringing a drug to market and therefore indirectly, to its price. It can also be a barrier to global consolidation around a smaller number of regimens, and most importantly to access to new and better medicines, since the necessary medicines are not always registered. The pharmaceutical company Abbott, for example, cited ‘broad registration’ as one of its measures to ensure access to medicines in developing countries.

Streamlining drug registration in developing countries could help reduce this barrier to access. Boehringer Ingelheim and GlaxoSmithKline (GSK) both cited regional registration as a way of ensuring that the newer drug reach developing markets more quickly. GSK made the point that many of the drugs waiting for national approval have already been approved by the world’s most stringent regulatory authorities, such as the FDA or the WHO and there could be significant savings by not repeating such an exercise nationally. However national registration is often seen as a matter of sovereignty.

39 Written evidence by CAFOD

40 Written evidence by CHAI and Boehringer, with specific reference to paediatric recommendations.

22 41 Written evidence by the charity Ace-Africa.

A less controversial option currently being explored by DFID, WHO, Gates, Clinton and NEPAD (The New Partnership for Africa's Development) is the harmonisation of drug registration templates which would mean that companies could provide the same data in the same format to all countries, which would speed up the process. Funding for technical support for individual countries whose registration system is particularly inefficient would also be useful. Such work would need to be done in communication with the pharmaceutical companies who have direct experience of dealing with the registration process.

Fast track registration is being used in Nigeria, according to evidence from CHAN Medi-Pharm Ltd., to expedite the entry of new medicines to market. However this is not yet being used for HIV, which CHAN believe is a missed opportunity in Nigeria and a system that could be used elsewhere in the world.

Another registration issue pushing up the price of medicines and slowing down access is PEPFAR's rule that it will only buy medicines that are FDA approved, as well as WHO approved. The other major drugs purchasers only require WHO approval. Some of the generic versions of ARVs are approved by the WHO but are still pending FDA approval. In these cases, PEPFAR buys the more expensive originator company versions, if available, or otherwise waits for FDA approval.⁴²

Process or Dosage Optimisation

The Clinton HIV/AIDS Initiative has been working with generic manufacturers to bring the cost of manufacturing key HIV medicines down. Dosage optimisation ensures the active ingredient, which is the most expensive part of the pill, is delivered in just the right quantity and no more. Drug dosage can be reduced in one of two ways – either by conducting clinical trials to demonstrate that lower doses produce the same efficacy with equal or reduced toxicity, or by developing more efficient drug formulations to deliver the same amount of active ingredient to the active site in the body while loading less active ingredient in the pill. Another piece of important research has looked into improving process chemistry. This can dramatically lower the cost of production, especially for chemically complex drugs such as Tenofovir and the protease inhibitors. The section on research and development in this report highlights the need for funding for this important type of research.

Improved Market predictability – another means of reducing risk and therefore prices

Some drug companies raised market predictability as an opportunity for reducing costs in their evidence to the APPG. Evidence from DFID is that accuracy of demand forecasting and predictability of payment can be as important to suppliers as volume in setting prices.⁴³ Many countries procure haphazardly (often driven by unpredictable donor funds) and don't procure forecasted volumes. The pharmaceutical company, Gilead, said in its evidence:

"The current state of forecasting demand for HIV drugs poses a significant challenge to delivering medicines and encouraging sustainable programs. A crucial planning element is donor coordination between the Global Fund, PEPFAR, UNITAID, the Clinton Foundation and other relevant partners. Of note, the competitive tender process often required can have a strain on forecasting depending on how it's implemented. For instance, there is a high level of uncertainty surrounding tender issuance and volumes quoted may not be ultimately procured. Lead times are variable, making supply chain planning and execution difficult. The opportunity we see in this arena is to establish support for an accurate, global demand forecast plan to be utilized by manufacturers to ensure consistent product availability for patients most in need."⁴⁴

42 There is an interesting statement from the Ecumenical Pharmaceutical Network (EPN) on this issue at http://www.healthgap.org/press_releases/04/100704_EPN_PEPFAR_statement.doc

43 Discussions with Saul Walker, Senior Access to medicines Policy Adviser, DFID, June 2009.

44 Written evidence to the APPG

Summary (Part B)

Higher volumes achieved by consolidation around WHO-recommended regimens and streamlined drug registration are an opportunity for achieving economies of scale. However, countries cannot be expected to include regimens that are not suitable for their citizens or appropriate to their resources on their 'Essential Medicines Lists'. A combination of more funding for relevant clinical trials and support to analyse the economic and public health costs and benefits of various treatment options are needed. Other opportunities for cost reduction are process or dosage optimisation and improved market predictability.

Recommendations:

1. UNITAID, and the big funders of drugs purchasing, such as the Global Fund for AIDS, TB and Malaria, have a good chance of breaking the 'chicken and egg' volume/price deadlock, if they indicate they are willing to fund the more expensive drugs, such as Tenofovir.
2. The WHO also has an important role to play in ending the dead-lock by promoting its recommendations more clearly and updating them regularly.
3. Developing countries will be more willing to change their preferred drugs if they can be shown to be appropriate to them. Funding for clinical trials is needed to produce data showing the relative efficacy of various treatment options in a resource-limited context and where there is a shortage of health care workers to help deliver them.
4. Donors could consider setting up an international facility based on the UK's National Institute for Clinical Excellence (NICE). The International Institute of Clinical Excellence would help countries to decide which drugs should be prioritised to meet their national health goals.
5. Efforts to harmonise the regulation of drugs will improve access but must be negotiated with sensitivity, to ensure willingness to participate. It would be helpful if such efforts were championed by a developing country or regional organisation. This could speed up the delivery of newer, better drugs to market and save money.
6. PEPFAR should end its policy of requiring FDA approval as well as WHO approval of the medicines it supplies.
7. Key donors such as the Global Fund, PEPFAR and UNITAID should continue to work to clarify and coordinate their tender processes and lead times and engage with all the relevant companies that comprise the pharmaceutical industry to provide improved global demand forecasting.

Section 5:

HIV-related Research and Development needs and the impact of patents

For drugs with a commercial market, income from patents is the incentive to invest in research and development. Thanks to this incentive, millions of pounds of investment by originator companies have resulted in the development of life-saving HIV drugs that otherwise might not exist. This point is commonly made by originator companies that are unhappy about the use of patent flexibilities discussed earlier in this report. Patents from such drugs are earning revenue from the developed country market.

Drugs for developed country markets can be refined into drugs better suited to the developing world. However, thus far the patent incentive alone has not delivered the necessary adaptations of medicines or new medicines for a developing country market. There are a number of areas where new diagnostics, completely new medicines or new formulations of medicine are urgently needed. These are outlined below. Since the simple patent system is not addressing these research needs, this report considers alternative or additional incentives to drive R&D investment. In particular it considers whether, in the context of diseases of poverty, the cost burden of R&D can be borne by someone other than the purchaser who pays through the price of the drug.

There is a need for the following new medicines:

- More single tablet, fixed-dose versions of the WHO recommended first line ARV combinations are needed. Fixed dose combinations are important because they are easier to take than taking several pills, separately in different quantities, and at different times of day. They therefore improve adherence and are also easier and cheaper to ship and store.
- More paediatric HIV drugs are needed. There is a lack of investment into medicines that are appropriate for children, because of the very limited commercial, developed country market for them. Children's HIV medicines do exist, but of the 22 antiretrovirals approved by the US FDA and currently available, six are not approved for paediatric use and seven are not available in paediatric formulations.⁴⁵ There is an urgent need for new formulations of HIV medicines for children and for drugs that are easier to use such as small tablets.
- Diagnostics are the third area where new developments are needed. A simple CD4 based diagnostic that is cheap and easy for staff to use with minimal training would enable people living with HIV to be diagnosed and treated earlier and more successfully.
- A simple point of care viral load test would enable medical staff to assess the effectiveness of a given HIV treatment on an individual so that treatment can be changed when it stops working (the shift from first to second line treatment). Currently treatment failure is being diagnosed late, this is not only bad for an individual's health; there is also an increased risk of transmission of resistant forms of HIV.
- Existing diagnostics for children under 18 months are also inadequate. The normal anti-body tests cannot be used on these children and under the current system a blood test is taken and then sent off to a laboratory for analysis. It can take up to eight weeks to get a response, and many children are never brought back by their carers for a result, thus many children are left untreated. Early treatment is key to their survival rates. Without treatment, half of the children with HIV/AIDS will not survive beyond the age of two.
- Similar research and development needs exist for tuberculosis, a disease which kills 23% of people who die with AIDS.⁴⁶ Better TB diagnostics are required, because the currently-used sputum test is unreliable, time consuming and requires trained clinicians. HIV can mask the TB in a sputum test and so many people with HIV who take the test get a negative result for TB, even if they are in fact infected. TB and malaria R&D are particularly neglected because relevant medicines have an even lower commercial market than for HIV.

45 UNITAID 'The Medicines Patent Pool Initiative' 2009 http://www.unitaid.eu/images/projects/PAT-ENT_POOL_ENGLISH_15_may_REVISED.pdf

46 WHO 2009 <http://www.who.int/tb/hiv/faq/en/>

Research and development needs are not limited to treatment and diagnostics; HIV prevention technologies have the potential to transform the global epidemic in a way that treatment does not. The International AIDS Vaccine Initiative (IAVI) and the International Partnership for Microbicides (IPM) are examples of important public/private partnerships which need long-term investment. The UK Government has committed to increasing its investment in research for AIDS vaccines and microbicides by 50% between 2008 and 2013, which is to be welcomed.

For a full list of missing HIV medicines see the WHO report of the 17th Expert Committee on the Selection and Use of Essential Medicines.⁴⁷

Missing data

As well as missing medicines and diagnostics there is missing data about the suitability of some of the existing medicines for a developing country context. Clinical trials are often designed with a view to registration in the developed world, to capture maximum commercial benefits. There are few studies supporting appropriate use of drugs for children. Information on whether the drug is safe for use by people with common co-infections in developing countries, such as TB, or for people who are taking anti-malarials is also missing. For example the HIV drug Efavirenz needs to be studied urgently in children below three years old so that TB/HIV co-infected infants can use it without drug interaction problems while taking TB drugs.

The lack of capacity to run clinical trials in developing country settings is holding back the development of new medicines specifically designed for such environments.

GlaxoSmithKline said in its evidence to the APPG, "An area of increasing concern in the broader regulatory context is the capacity in developing countries to conduct clinical research. Clinical trials require suitable sites with trained personnel, sufficient resources & infrastructure, and appropriate regulatory & ethical oversight. As the pipeline of the product development partnerships mature, the capacity of the few suitable clinical facilities, especially in Africa, will be dangerously over-stretched. The Government should work with the Medical Research Council, developing countries, and other stakeholders, including the industry, to identify ways to help address this major concern."

This concern was also raised directly with us by Professor Diana Gibb from the Medical Research Council and is reflected in the George Institute's G-Finder report.⁴⁸ There is also a need for post-registration research, to identify any new problems with a medicine that is already being used that may be particular to a developing country, or a population sub-group.

What is the impact of patents on research?

Most of the fixed dose combinations used in developing countries have in fact been developed by generic manufacturers in response to market demand, not patent incentives. The most important example of this is Trimune which is the generic fixed dose version of the basic combination that has been referred to frequently in this document – Lamivudine, Stavudine and Nevirapine. This was developed by the Indian company, Cipla, who then partnered with the Medical Research Council to make the first fixed dose combination for infants, Baby Trimune. These medicines have not been patented and have demonstrated that this type of research and development can be viable, and indeed profitable, without patents.

Patents can also create barriers to the development of new fixed-dose and co-packaged therapies, because of the cost and complexity of dealing with three different patent holders. Overly-broad patent rights may also result in so-called "patent thickets", which are dense webs of patents on one product that may be owned by a multitude of different parties.⁴⁹ Companies seeking to use technology for the development of new and superior products have to pay considerable licensing fees or challenge blocking patents in costly and lengthy litigation.⁵⁰

This looks likely to be a serious problem for Indian generic manufacturers who developed the fixed dose combinations referred to above, but since becoming TRIPS-compliant in 2005 now face stricter patent laws which will limit their ability to develop new combinations.

47 WHO 'Report of the 17th Expert Committee on the Selection and Use of Essential Medicines' 2009 http://www.who.int/selection_medicines/committees/expert/17/WEBuneditedTRS_2009.pdf

48 The George Institute for International Health "Neglected Disease Research & Development: How Much Are We Really Spending?" G-Finder Feb 2009 <http://www.thegeorgeinstitute.org/>

What incentives can there be for research other than patents?

Research and development is an expensive business and if it is not to be funded through patents, and ultimately the consumer, the funding will need to be found elsewhere. Suggested models of encouraging innovation in HIV and neglected diseases can broadly be divided into 'push' and 'pull' mechanisms.

Push mechanisms reduce the risks and costs of investment in R&D. They include direct funding of research, and tax credits, both of which have been used by the UK government.

Many of those who responded to the APPG enquiry felt that public-private partnerships whereby governments or philanthropic organisations could help fund private companies to undertake research would be useful. DFID already gives important sums to the Medical Research Council however this money is spent on early academic university-based research or final stage research such as field trials. In the case of HIV medicines and diagnostics there is no DFID funding for the expensive but important middle stages of treatment development - these are usually done in the private sector. The Global Fund for AIDS, TB and Malaria does not invest in research into the development of medicines at all. The Bill and Melinda Gates Foundation is the exception, as it invests in HIV research and development.

Missed opportunities for cost-savings

The Clinton HIV/AIDS Initiative (CHAI) felt that the type of research they are facilitating on optimising manufacturing processes or levels of active ingredient in a medicine is under funded. This type of research was mentioned in Section 4 B as a way of reducing the cost of medicines. In written evidence to the APPG, they said:

"Incentives and funding for the optimization of existing ARVs for developing world purposes—what can be thought of as 'downstream' or post-marketing R&D—is a major gap in today's HIV/AIDS funding landscape.there are virtually no donors prepared to fund the optimization of existing drugs. Opportunities such as dose optimization, reformulation, and packaging innovations must be pursued at-risk by suppliers or others seeking to create value in these ways.

Increased funding for such R&D would create potentially tremendous value. CHAI has identified a range of opportunities for future impact through this kind of product optimization, but has been largely unable to find funders to connect with potential implementers. Financial support could come in the form of 'push' funding—ie, grants for R&D projects—or 'pull' funding such as advance market commitments or prizes. New philanthropic ventures and novel financing mechanisms such as UNITAID offer the best hope for an influx of funding in this sphere." (CHAI)

The main drawback to 'push' mechanisms, such as direct funding, is that they require funders to make a judgement about which research bodies are most likely to achieve the needed results, and sometimes the recipients of funding do not deliver.

'Pull' mechanisms in contrast, create an extra incentive to achieve the result (such as a new medicine) with the benefit only delivered on achievement. Examples of such mechanisms include prizes for the first researchers to come up with a specified innovation, advanced market commitments or tax credits on sale of a certain product which is yet to be developed.

Prize funds are one of the mechanisms attracting the most interest from those seeking to catalyse new research in HIV and were cited as a solution to R&D needs by respondents to the APPG enquiry.⁵¹ Prizes have been used for hundreds of years to spur innovation, and history shows that prizes often generate total R&D investments greater than the value of the prize. However, they do not always work and the sums offered

49 A single vaccine for example could include patents on: the antigen needed to produce the proper immune response, including its DNA sequence and particular expression; the adjuvant, which is used to facilitate a person's response to an antigen, the excipient, which is the substance and antigen and adjuvant are stored in; the vaccine itself; and finally, its method of delivery. <http://www.ip-watch.org/weblog/2008/04/22/experts-debate-policy-on-patent-landscapes-for-life-sciences>

50 See "The arms race. Companies are preparing for the intellectual property battle", in: The Economist, 22 October 2005, special edition "A market for ideas. A survey of patents and technology", pp. 8/9

need to be substantial. The Rockefeller Foundation for example offered a \$1 million prize in 1994 to develop a simple point of care diagnosis for STIs, which was never claimed, possibly because it simply was not large enough to act as an incentive to conduct expensive research.⁵²

The need to offer substantial funding has led some to propose that prizes should be offered on the basis of donations from multi-national sources, coordinated perhaps by the WHO. Oxfam has called for a Global Fund for Research and Development.⁵³ However, prizes tend to favour companies that can commit significant financial resources upfront, rather than smaller companies, that may have the necessary skills but lack sufficient cash flow to put them into practice.

There is also a precedent in the use of 'Advanced Market Commitments', another form of pull mechanism. The pharmaceutical company, Boehringer, suggested these should be used in HIV in its evidence to the APPG enquiry. An Advanced Market Commitment has been developed under the auspices of GAVI, the Global Alliance for Vaccines and Immunisation, to encourage the development of a vaccine for pneumococcal disease. It is too early to tell how successful such investments will be.

Less formal ways of indicating a solid market for a potential new medicine can also be effective. There has already been some progress in this area, with UNITAID acting as a major buyer and stating the medicines it feels need to be developed and that it would like to buy. The Global Fund's purchasing power is also creating a credible market for HIV medicines.

Patent Pools

A new mechanism, called a 'patent pool' is being proposed by UNITAID as a method of catalysing the development of some of the missing medicines identified at the beginning of this section. Patent owners put their patents in a 'pool' and allow others who need access to those patents to use them in exchange for a royalty payment. Patent pools have already been used to drive forward innovation in different fields of technology, for example MP3 players, but their use in pharmaceuticals is a new development.

The pool is designed to make it easier for researchers who want to develop combination therapies because they can access permission to use the component drugs from a single place, rather than having to negotiate company by company. Those using the patents still pay a royalty to the patent holder, administered by the pool. It is also designed to reduce prices of existing medicines by allowing generic manufacturers to produce drugs on payment of a royalty. As discussed in Section 4A, it is hoped the pool will mimic the situation in India before the country brought in a TRIPS patent regime in 2005, so that affordable second line drugs can be produced.

Who supports the idea of the Pool?

The development of this proposal by UNITAID is being encouraged by the UK Government⁵⁴ and WHO⁵⁵ and supported by all the major international development charities in the UK. However its success depends entirely on the willingness of patent owners to put their patents into the pool. The All Party Parliamentary Group invited organisations, including pharmaceutical companies to give their views on the feasibility of the pool.

GlaxoSmithKline is in favour of the concept of a patent pool for neglected diseases and has set up its own version covering TB and malaria and other diseases prevalent in the developing world. Its new Chief Executive put on record his support for the concept in the Guardian, saying "I think it's the first time anybody's really come out and said we're prepared to start talking to people about pooling our patents to try to facilitate innovation in areas where, so far, there hasn't been much progress."⁵⁶ However as yet, GSK has not agreed publicly to put any of its HIV patents in to its own pool or the UNITAID patent pool.

Their written evidence to the APPG enquiry said: "For HIV, we believe that extensive research is already underway, and thus it is not a neglected disease. Millions of dollars are ploughed into research into HIV every year by the pharmaceutical industry. To improve access, we already have an extensive voluntary licensing

51 H Wong & M T Isbell, IAVI, April 2009 'Spurring innovation for the Development of HIV/AIDS Technologies.' http://www.iavi.org/Lists/IAVIPublications/attachments/1377/IAVI_Spurring_%20Innovation_for_the_Development_of_HIV_and_AIDS_technologies_2009_ENG.pdf

52 ibid

53 Oxfam International, 'Ending the R&D crisis in Public Health' November 2008

54 Hansard, 25/3/09, DFID PQs Ivan Lewis MP, DFID

28 55 Verbal evidence to the APPG, Jos Perriens, Coordinator Systems Strengthening and HIV(SSH) Unit, WHO

programme for HIV across Sub Saharan Africa, involving eight licensees. These licensees are free to develop FDCs and paediatric versions and we believe this is a much simpler approach than the creation of a patent pool... All our ARVs are also available at not-for-profit prices in all Least Developed Countries and Sub Saharan Africa. We therefore do not see the need to include our HIV patents in any pool.”

However these voluntary licensing schemes have been in place for several years and there are still significant research gaps. Furthermore, where fixed dose combinations (FDCs) include medicines from a number of different patent holders, a scheme by a single company, or even two companies⁵⁷, is still more difficult to use than a ‘one stop shop’ solution.

There is strong political pressure for companies to participate in the pool, with over 100 UK MPs signing an Early Day Motion (a parliamentary petition) on the subject and a public campaign supported by over 22,000 signatories.⁵⁸ The UK Government has also publicly called for “pharmacological companies to respond positively to this initiative [the patent pool] and join forces so that we can make the contribution to driving down prices and improving access to HIV/AIDS drugs.”⁵⁹

Summary

Patents are an important incentive for R&D in developed country markets, but do not generally drive investment into HIV medicines specifically needed by developing countries. Indeed, they can sometimes hinder such research.

R&D is expensive and if it is not to be funded by patent income, incentives must be found elsewhere. Public private partnerships and direct research funding are possible sources, as are prize funds, tax credits or advanced market commitments.

A patent pool is another option that rewards the patent holder whilst reducing barriers to further R&D by researchers who wish to refine a product for a developing country market. It would also enable the type of generic production which has made HIV medicines available to three million people and which generated the first ever fixed dose combinations, to continue.

Recommendations on encouraging R&D

1. The private sector has excellent skills and experience in translating early academic stage research into usable products. They are more likely to engage in this expensive, risky process, if there are incentives for them to do so. Proposals to stimulate R&D need to ensure adequate financial incentives.
2. There is an urgent need for improved capacity for clinical trials in developing countries. Donors not currently funding such work should consider doing so, in collaboration with organisations such as the Medical Research Council, academic institutions and private companies.
3. Pharmaceutical companies and other patent holders should sign up to the UNITAID patent pool to enable new fixed dose combinations (FDCs) and paediatric versions of HIV drugs, in return for a fair royalty on their patents.
4. HIV funders should consider investing money in late stage research, a process that the Clinton HIV/AIDS Initiative has begun to facilitate, on the basis that such research has already proved its worth and that there is scope for further gains.
5. DFID, in communication with its counterparts from other donor countries and with UNITAID, should look into the workability of a prize fund for key missing medicines and diagnostics.
6. In a global economic downturn there will be a temptation to divest from ambitious research projects such as an AIDS Vaccine, but this should be resisted because long-term stability is essential to make gains from investments thus far, and because new prevention technologies have the potential to revolutionise our response to HIV and minimise the epidemic.

56 As reported, Guardian ‘Drug Giant GlaxoSmithKline Pledges Cheap Medicine for the World’s Poor’, 13th Feb 2009, <http://www.guardian.co.uk/business/2009/feb/13/glaxo-smith-kline-cheap-medicine>

57 GSK and Pfizer are now working together on ARVs

58 22,696 people have signed up to ‘Join the Push for the Pool’ part of The Stop Aids Campaign.

59 Hansard, 25/3/09, DFID PQs Ivan Lewis MP, DFID

Section 6:

Conclusion

It took political activism almost a decade ago to make life-saving drugs available to the poor in developing countries. People with HIV took to the streets and to the court room to fight for the right to treatment and were supported by international NGOs all over the world. The work they started is not over. Only a third of those who need it are on treatment and this treatment will not work for them forever. Political activism is needed once more to ensure that the next generation of drugs is available to the world's poorest in future. We must not sleep walk into a situation where treating even a small proportion of those with HIV is unaffordable.

Prevention activities take time to feed through into lower rates of infection and therefore the high numbers of people in need of treatment predicted in this report are almost inevitable. What need not be inevitable are spiralling treatment costs. All actors must be involved in preventing this, including the UK government, NGOs, international organisations, the private sector and developing country governments.

Pharmaceutical companies have a particularly important role to play. Generic production has single-handedly driven a huge reduction in the price of life-saving medicines enabling millions of poor people to access treatment. The extent to which generic companies are allowed to produce new HIV medicines in the future is critical, and it will depend on the willingness of originator companies to cooperate. So originator pharmaceutical companies must rise to meet the challenge of the public's expectations by allowing their drugs to be made more cheaply for use by developing countries, and signing up to important mechanisms, such as the UNITAID patent pool.

However, casting originator pharmaceutical companies as the enemy in the access to medicines debate takes no account of the essential role they have played in developing the treatments that so many rely on today. They will and must play a continuing part in responding to HIV as it mutates and throws up new challenges in the years to come.

We must also recognise that whilst it is right that companies should invest some of their profits in research and development to improve their medicines for the developing world market; if they are to address some of the biggest challenges, it may take additional or different incentives. DFID, its counterparts and the major international funders need to sustain (and in some cases where there is no current R&D spend, establish) research and development funding, particularly for clinical trials, and make full use of incentives with a positive track record, such as prize funds.

HIV is with us for the long-term and calls for significant financial commitments. As the UK Government's AIDS strategy acknowledges:

"No Low-Income Country with a hyper-endemic or generalised epidemic has yet come close to achieving self-sufficiency in delivering an effective AIDS response, even in the medium term. The conclusion is stark – Universal Access cannot be achieved in these countries without sustained donor assistance. The international community must therefore maintain its commitment to supporting AIDS responses in the long term."⁶⁰

Donor fatigue is a serious risk with such a long-term project. Governments, charities and international organisations such as UNAIDS, therefore need to work quickly on a shared message to take the access to HIV medicines work beyond 2015.

This report focuses on treatment, but in highlighting the complexities and expense of a lifetime on medicines, the conclusion that prevention must be key to any long term response is inescapable.

Nonetheless there are clear milestones to be achieved to diffuse the treatment timebomb; affordable, quality, first and second line medicines; access to related products for co-infections; more paediatric treatment options; affordable diagnostics to ensure adults and children are diagnosed in time to prevent permanent damage to their immune systems; and affordable, effective, prevention of mother-to-child medicines. We should waste no time in achieving them.

60 DFID 'Achieving Universal Access- The UK's Strategy for Halting and Reversing the Spread of HIV in the Developing World' 2008. <http://www.dfid.gov.uk/Documents/publications/achieving-universal-access.pdf>

A Stop AIDS Campaign activist demonstrates his support for the Patent Pool. Photo printed with permission from Emma Critchley.



Acronyms

AIDS	Acquired Immunodeficiency Syndrome
APPG	All Party Parliamentary Group
ART	Antiretroviral Therapy
ARVs	Antiretroviral Medicines
DFID	The Department for International Development (UK)
FDA	The US Food and Drug Administration
FDCs	Fixed Dose Combinations
Global Fund	The Global Fund for AIDS, TB and Malaria
HIV	Human Immunodeficiency Virus
ICTSD	International Centre for Trade and Sustainable Development
ICW	The International Community of Women Living with HIV
LDCs	Least Developed Countries
NEPAD	New Partnership for Africa's Development
NGOs	Non Governmental Organisations
PEPFAR	The President's Emergency Fund for AIDS Relief
PMTCT	Prevention of Mother-to-Child Transmission
R&D	Research and Development
STIs	Sexually Transmitted Infections
TRIPS	Trade Related Aspects of Intellectual Property Rights
UNAIDS	The United Nations Joint Programme on HIV/AIDS
UNITAID	International Drug Purchase Facility
WHO	The World Health Organisation
WIPO	The World Intellectual Property Organisation

Organisations that contributed to the APPG enquiry

Developing country based charities

- ACE Africa
- Christian Health Association Malawi
- Chan Medi-Pharm Ltd
- Treatment Action South Africa
- Nairobi Network of Post Test Clubs
- HAI Africa
- Living Hope Organisation

UK based charities

- CAFOD
- Oxfam
- Advantage Africa
- ICW
- Stop AIDS Campaign
- International AIDS Alliance
- World Vision
- Children's Investment Fund Foundation
- NAM
- Medecins Sans Frontieres

Private Sector

- SAB Miller
- GSK
- Gilead
- Boehringer Ingelheim GmbH
- Johnson and Johnson
- Abbott

Other

- Clinton HIV/AIDS Initiative
- Global Fund for AIDS, TB and Malaria
- Medical Research Council (MRC)
- London School of Hygiene and Tropical Medicine
- GAVI
- University College London
- Imperial College London

Government/ International Governmental Organisations

- DFID
- International Centre for Trade and Sustainable Development
- South Centre
- World Health Organisation
- UNAIDS
- UNITAID
- World Trade Organisation
- UK Mission to the UN in Geneva
- UNICEF
- UNCTAD

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