Global Health

and the Pharmaceutical Industry

abpi

A Welsh translation of the introduction to this booklet can be found at **www.abpi.org.uk/publications**

The Association of the British Pharmaceutical Industry (ABPI) is the trade association for more than 75 companies in the UK producing prescription medicines. Its member companies research, develop, manufacture and supply more than 80 % of the medicines prescribed through the National Health Service. Medicines discovered, researched and developed in Britain bring health benefits to millions of people around the world.

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Introduction

Right now, in countries across the world, millions of people are dying unnecessarily each year from diseases that can be easily prevented or effectively treated.

Conditions like diarrhoea and respiratory infections that have either been largely eradicated, or are considered minor, in wealthy countries continue to flourish and exact a punishing death toll in poorer countries.

Global poverty is an issue that concerns everyone – and nowhere more clearly demonstrates the damage poverty inflicts than in health. Lack of access to basics like food, decent housing and clean water mean people are more susceptible to falling ill. Poverty also means that the health infrastructure we take for granted in richer countries such as hospitals, health clinics and trained health workers is simply too stretched if available at all. Ill-health means that populations are less economically active and productive than they could be which, in turn, locks people into a vicious cycle of poverty.

As a global industry whose aim is to improve health, it is a clear responsibility of the pharmaceutical sector to do its part in addressing this need, alongside governments, philanthropists and other major corporations. Access to the right treatment is vital for many of the world's poor – but this must be combined with addressing the causes of poverty.

The debate about how best to advance health in developing countries condenses all of the issues – at once stark, emotive, practical and structural – that arise when developed and developing world economies meet. Pharmaceutical companies working in western market-based economies have proven extremely effective at delivering huge improvements in health over the past 50 years. Making the same impact in poorer countries where the market alone cannot deliver is difficult, but the industry is not shying away from this challenge. Dealing with these problems requires sophisticated approaches and long-term commitment from all partners across governments, international organisations, voluntary sector and private enterprise. Affordability of treatments is important, but is only one of many problems that need to be overcome – and by no means the most difficult – if greater access to quality healthcare is to be achieved.

The global pharmaceutical industry commitment to tackling disease in the developing world is long standing, with medicine donation programmes and vaccination schemes dating back to the 1980s. Since 2000, this work has escalated dramatically as many companies have become involved in public-private health partnerships. More than 120 of these partnerships have been established since the start of the millennium, and these have provided enough health interventions to treat more than 500 million people. The value of these pharmaceutical industry donations and investments over the past six years has totalled more than £2.45 billion[i]. UK-based companies are among those leading the way in both the effort and resources they dedicate to tackling developing world diseases and are among the most forward thinking in how these efforts can be made more effective.

This publication from the Association of the British Pharmaceutical Industry (ABPI) explains the global industry's approach to some of the complicated issues surrounding world health, demonstrates the work that companies are already undertaking to improve health in poor nations, and looks ahead to what more may be done in the future.

Dr Richard W Barker
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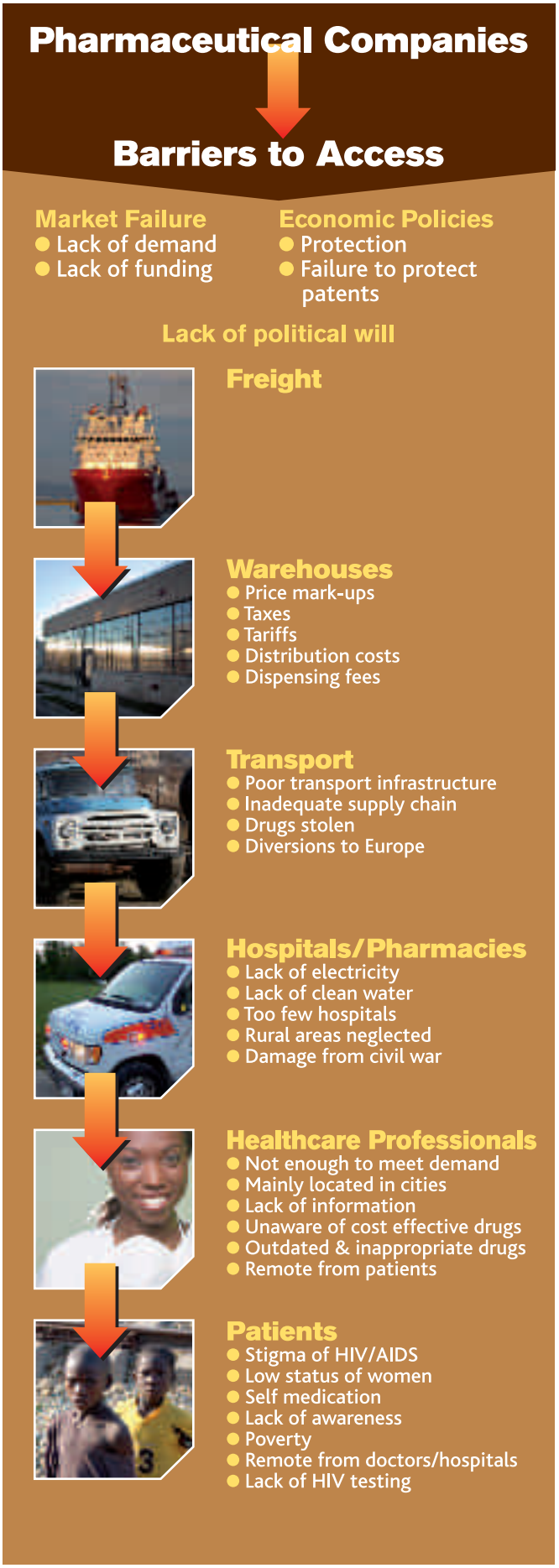
Establishing the scale of the problem

The figures, and the inequities they reveal, are alarming:

- There are estimated to be up to 500 million cases of malaria per year – causing up to three million deaths[ii].
- The global HIV/AIDS epidemic is estimated to have taken some three million lives in 2006 and around 40 million people live with the disease[ii].
- Tuberculosis, an infection that has taken on new and even deadlier forms in those whose immune system has been ravaged by AIDS, is carried by one third of global population and kills two million a year[iii].
- The childhood death rate in high-income countries is lower than 20 per 100,000 – in sub-Saharan Africa it is more than 1,600[iv]. Around a third of these deaths are caused by respiratory and diarrhoeal infections[v].
- The Africa Region of the WHO suffers more than 24% of the global burden of disease, but has only three per cent of the world's health workers[vi].
- In high-income countries, around 70% of people can expect to live beyond 70; in low-income countries only 20% can expect to reach that age[vii].

Much attention has rightly been focused on the disease burden posed by malaria, HIV/AIDS and TB. But it is telling that respiratory and diarrhoeal infectious diseases remain bigger killers. These are conditions where full cure is easily possible with basic health services, the treatment cheap and well-established in generic production for decades, and yet the appropriate care is still not getting through. In fact, 95% of the medicines listed on the World Health Organisation's Essential Medicines List are not covered by patents and are thus available for generic production – yet a third of the world's population is denied reliable access to them[viii].

Furthermore, it is not just in the world's poorest countries where inequalities of health are apparent. The divide in access to healthcare can be acute in middle-income nations too.



How AIDS focused the debate

In the case of HIV/AIDS, the complexity of the problem we face is daunting and defies all attempts at easy answer. The socio-economic challenge that the AIDS epidemic presents have reached to the very heart of the debate about the global response to health in the developing world. It is the challenges raised by this particular disease that has mobilised richer nations to focus on the health of the whole world and what more might be done to improve fairness.

HIV, the single largest modern epidemic to hit mankind, affects both developed and developing worlds. The only treatment options currently available slow the development of the disease – that is, they can extend life and wellbeing but not cure the disease – are expensive to develop and difficult to apply in all but the best clinical settings. An effective vaccine is the target of increasing efforts, but is probably at least ten years away.

Furthermore, many of the medicines require developed health systems to deliver them and for the patient to be in good physical and nutritional condition for them to be effective.

Even the fact of sexual transmission of HIV brings into question controversial and sensitive cultural and social differences between countries that influence how the disease may be prevented. Other social factors, such as fears of stigma and discrimination, often prevent people from seeking treatment.

At every level – cultural, financial and scientific – the challenge of HIV/AIDS has absorbed our attention because it most starkly demonstrates the fault lines in health between rich and poor.

Working in partnership

The pharmaceutical industry feels strongly that partnership between the public and private sector can overcome the many complicated interlinking issues of poverty and disease. The pharmaceutical industry research model has clearly delivered a quality and choice of medicines that have improved lives and enhanced society, and the business conditions that have enabled this must be protected. Equally, NGOs, governments and inter-governmental organisations are best placed to ensure that the benefits of these medicines reach communities where the market alone cannot deliver. Sophisticated partnerships are now developing that aim to maximise the talents and effectiveness of both.

Beyond this, corporate philanthropy and vision from extremely wealthy individuals (most notably in recent years Bill Gates and Warren Buffett) have also brought fresh impetus to these collaborations.

CASE STUDY 1:
Partnering on health system solutions: Pfizer and the Infectious Diseases Institute

The Infectious Diseases Institute (IDI) at Makerere University in Kampala, Uganda is a state-of-the-art regional centre for treatment, training, research, laboratory and diagnostic services that meets the unique challenges of the African HIV/AIDS epidemic.

The IDI is the result of a partnership between Pfizer, Makerere University, international infectious disease experts, the Ugandan government, and NGOs. The focus

Infectious Diseases Institute, Specimen Accessioning/ Processing Lab, Kampala, Uganda.

of this regional training and treatment centre is to strengthen local capacity in HIV/AIDS care. Training healthcare professionals in the latest treatment options is an important component in fighting the HIV/AIDS crisis and infectious disease experts based in the Institute train doctors from many African countries in the prevention and treatment of HIV/AIDS.

The Institute has a significant impact in Africa, striking at the core of the AIDS epidemic by providing extensive training to healthcare providers and advanced treatment methods to patients, including:

- *The provision of enhanced HIV care for adults, children and families, including anti-retrovirals and prophylaxis for opportunistic infections;*
- *Education and training for African physicians and healthcare providers in HIV care and prevention;*
- *A state-of-the-art diagnostic laboratory to monitor HIV therapy and to support diagnosis of opportunistic infections, tropical diseases and sexually-transmitted diseases;*
- *Clinical research to identify the best approaches for patient care, including directly observed therapy and once-a-day treatment regimens.*

Since 2004, the IDI has trained more than 1,200 healthcare providers from 26 African countries. So far the centre has delivered care to approximately 10,000 patients.

In this building, known as the Inifectious Diseases Institute, and subsidised by Pfizer Inc, HIV-positive patients can receive free medical care.

CASE STUDY 2: Helping NGOs become more effective and spread best-practice

AstraZeneca and VSO

AstraZeneca has recently entered into a partnership with VSO (Voluntary Service Overseas). VSO is an international development charity that works through volunteers. It has 50 years' experience in recruiting, placing and valuing volunteers and is by far the largest independent volunteer-sending agency in the world with, at any one time, 1,500 skilled professionals working in 34 countries. VSO has six development goals, one of which is health.

The partnership will have two main features:

1. *AstraZeneca will give strategic and financial support to VSO's health goals and assist the VSO's work with governments and other local organisations, such as NGOs, to strengthen capacity in order to deliver better health outcomes for those most in need across the developing world.*

2. *AstraZeneca staff will be given the opportunity to take part in international placements as volunteers with VSO.*

Abbott and BIPAI

Abbott, through its charitable foundation the Abbott Fund, supported a Romanian AIDS programme in collaboration with Dr Mark Kline of the Baylor College of Medicine's International Paediatric AIDS Initiative (BIPAI). At the time that the programme began, Romania had very

limited medical resources and an overwhelming paediatric HIV caseload. It was, and remains, the only country in the world where paediatric cases outnumber adult.

The Abbott Fund worked with BIPAI to establish a model paediatric clinic in April 2001 and not only offers HIV outpatient care and treatment for more than 600 patients but also provides psycho-social support, select residential care and community education.

The BIPAI-Abbott Fund paediatric AIDS clinic model established in Romania has proven so effective that it is being replicated throughout Africa and other parts of the developing world by the Abbott Fund and other donors. Besides the Romania clinic, other BIPAI clinics now operate in Malawi, Botswana, Lesotho, Swaziland, Uganda and, soon, Burkina Faso. As of March 2007, the programme is treating more than 12,000 children. This is the largest group of children in the world being treated for HIV by a single programme.

All in the global health community are increasingly aiming to avoid one-off donations or fixed-term 'model' health projects that allow conditions for those benefiting to slide back once the funding runs out. However well-meaning this kind of philanthropyis, past experience has shown that unstructured, uncoordinated aid which focuses on the donor's priorities over local needs can have serious unintended negative consequences for developing countries including damage or distortion of the local economy and aid-dependence. In health development programmes, sustainability is critical.

Only measures that build local capacity, reinforce the abilities of local health services and are aligned with local requirements will have lasting impact. It is approaches like these, focusing resources to deliver steady improvements, which pharmaceutical companies have initiated and supported in recent years. This involves more than supply of medicines and includes training health workers, education programmes, logistical infrastructure and research into neglected diseases.

CASE STUDY 3:
More than medicines – working to reduce disease burden

GSK's Personal Hygiene And Sanitation Education (PHASE) project is helping to reduce diarrhoea-related disease by encouraging schoolchildren to wash their hands. GSK established PHASE in 1998 and has so far invested more than $3.1 million in the programme. PHASE is run in partnership with AMREF, Save the Children and Plan International – as well as national Ministries of Health and Education in countries where the programme is active.

The programme has had impressive results so far. For example, a study by AMREF in Kenya showed that after four years, 88% of children from participating schools washed their hands after using the toilet, compared with 46% from non-participating schools. PHASE was extended to Mexico and Tajikistan during 2006 and now operates in a total of eight countries. The total number of children currently reached by PHASE is now estimated to be 375,000 and the aim is to reach one million by 2010.

GSK has a PHASE steering committee with representatives from partner organisations to help expand the programme into more countries. Bolivia and Indonesia are set to join, along with Kibera, Kenya: Africa's largest slum. This will be the first time PHASE has operated in an informal settlement, creating a model for improving children's health in one of the world's harshest urban environments.

Teaching children to wash their hands in Tajikistan reduces the incidence of desease.

Millennium Development Goals

In responding to global inequalities, the United Nations is currently committed to working towards reaching eight millennium development goals (MDGs) by 2015 – many of these relate to health, and the pharmaceutical industry can contribute to the efforts to achieve them. They are:

- Reduce childhood mortality by two-thirds in children under five.
- Reduce maternal mortality by three-quarters.
- Halt and begin to reverse the spread of HIV/AIDS, malaria and other major diseases.

Given the finite resources of governments, non-governmental organisations (NGOs), aid agencies and philanthropic and corporate giving, there are some difficult compromises that the global community must strike. Is it better to start by using these resources to provide a basic standard of healthcare across the whole developing world which can tackle the infectious diseases that cause much of the mortality burden, but know that this leaves populations uncovered for more complicated conditions? Or is it right to focus high quality health services that can provide palliative care for AIDS, but can only reach a limited number of people?

Regulation, corruption and trade tariffs

In many poor countries, there isn't capacity for strong civic regulators and authorities – and, therefore, corruption is a serious issue. This forms a significant barrier to medicines reaching the communities that need them and frustrates attempts to make access more equitable. Weak controls over supply chains allow counterfeit medicines to reach markets and leave patients untreated or even harmed by poor quality fakes. It also means that profiteers find ways to charge excessive mark-ups or re-import medicines donated or sold at low cost to poorer nations back into richer countries for profit.

Tackling corruption is a clear aim of governments (rich and poor) and the pharmaceutical industry fully supports this. In the UK, the government's Department for International Development (DfID) is investigating what role the UK might have in assisting developing countries tackle corruption through the Medicines Transparency Alliance (MeTA). MeTA aims to build transparency and accountability in the selection, procurement, sale and distribution of essential medicines to tackle the excessive mark-ups, corruption and mismanagement that cause good quality medicines to be either too expensive or unavailable for hundreds of millions of people in developing countries. The ABPI is a member of this partnership and industry is playing a leading role in helping to gather this vital information.

Internationally, the WHO is taking similar steps to promote transparency and ethical behaviour right along the medicine supply chain, and the industry is actively engaged in these efforts. One way industry can help is by participating readily in partnerships where access to treatment programmes is contingent upon achieving minimum standards of anti-corruption measures.

Another big issue to be resolved is the punitive taxation some developing countries impose on imported medicines which significantly increase the costs to patients. Import tariffs, VAT, port charges and local taxations of course exist in all nations – but their influence on affordability is very damaging in poor countries. In India, total duties and taxes add 55% to the retail cost of medicines; in Sierra Leone it amounts to 40%; and in Nigeria 34 per cent[ix].

In some very poor countries, trade tariffs represent a vital source of government income where collection of other taxes is difficult, so that encouraging these nations to recognise the negative effect of these charges specifically on medicines is an important task for the international community.

Planning for the future

More challenges lie ahead – lifting countries out of extreme poverty is not the end. Rapidly growing economies like India and China are seeing urbanisation on a massive scale as millions of previously rural

dwellers move into teeming and often badly polluted cities – without appropriate public health measures and health infrastructure, the death toll exacted by infectious disease can only grow.

Furthermore, as progress is made in dealing with acute infectious disease, increased populations are living with chronic diseases like diabetes, stroke or asthma. Chronic disease already vastly outstrips all other causes of death globally with more than 17 million dying annually from cardiovascular disease alone[x]. In the future, a strategy for effectively managing these conditions in developing nations will become ever more important.

It is also likely that there will be a greater focus on current health issues which remain under-discussed, with acute life-threatening diseases taking centre stage. Mental health, for example, is poorly managed, rarely reported on and carries huge stigma in many countries, and there is real need for improvement in treatment.

Cancer prevalence is global, and providing effective treatment in poor countries will become an increasing focus. In developed countries, the probability of being diagnosed with cancer is more than twice as high as in developing countries. The World Health Organisation reports that, in rich countries, some 50% of cancer patients die of the disease, while in developing countries, 80% of cancer victims already have late-stage incurable tumours when they are diagnosed, pointing to the need for much better detection programmes.

Once considered a "Western" disease, more than 50% of the world's detected cancer burden, in terms of both numbers of cases and deaths, already occurs in developing countries[xi].

CASE STUDY 4:
Tackling breast cancer in Ethiopia

In 2005, AstraZeneca started a pilot project in Ethiopia designed to build local capability in managing breast cancer – the second most common cancer among young women in that country. Ethiopia has only one breast cancer specialist for the entire population; there is no mammography; no easy access to chemotherapy or hormonal agents; no cancer screening and no national treatment protocol.

In its first 18 months, the programme has focused on strengthening diagnosis and treatment capabilities at Tikur Anbessa University Hospital in Addis Ababa (where the country's two oncologists are based). AstraZeneca's breast cancer medicines are also being donated. Ongoing objectives for the project include raising awareness of the facilities among healthcare professionals and strengthening the referral system; setting up an institution-based cancer registry; providing training for other physicians in Ethiopia; and establishing Tikur Anbessa University Hospital as a centre of excellence for diagnosis and treatment.

In the longer term, the sustainability of the project will be ensured through the educational initiatives established during the pilot, including the development of treatment guidelines, as well as assistance in putting in place mechanisms for future funding of the diagnostic and screening procedures.

If the pilot is successful, AstraZeneca hope that it will provide a model that can be replicated in other countries and other disease areas.

Key milestones include:

- *Establishing hospital guidelines for diagnosis, pathology reporting and treatment of breast cancer, including development of palliative care guidelines.*
- *Introducing mammography as an early diagnostic method for breast cancer.*
- *Introducing oestrogen/progesterone receptor tests.*

Intellectual property

The existence of patents and the eagerness of companies to defend this protection for their innovations are often cited as reasons why patients in developing countries do not get access to the treatment they need. Some in the global health community feel that patents are an insurmountable

and obvious barrier to providing access to treatment for the world's poorest. They contend that dismantling this system would provide affordable access to healthcare by widespread production of and trade in "generic" versions of medicines. So why are patents important? And why do companies feel the need to protect them?

The pharmaceutical industry invests the vast sums required for medicines R&D as a direct result of the protection provided by the patent system and believes a debate about global health which focuses on patent law does nothing to in a practical way assist those in need.

Medicines are expensive and time-consuming to invent and develop, with only a few possible medicines that are researched ever returning a profit – so trying to create them carries a great deal of financial risk. It takes ten or more years of painstaking research, including clinical trials, and on average costs more than £550 million for every new effective medicine developed. Many potential 'candidate' medicines are studied, but for every 10,000 molecules studied, only one will ever make it to patients. Of those medicines that eventually do get to patients, only one in three ever returns a profit on this research[xii]. It is these profitable medicines which, in effect, pay for the research into all the others.

Without patents to protect this investment, no company could justify this level of funding. No reliable publicly financed method has been found to invest these sums for the vast numbers of diseases and conditions that modern medicine treats on a daily basis – governments typically do not think that far ahead and academic institutions rightly focus on experimental science and do not have either the resources or the industrial development expertise. No public sector system could sustain the retention of the scientific talent required to undertake the R&D and manage manufacturing capacity.

Not only is affordable access possible without eroding intellectual property protection, but the removal of patents would also carry dangerous unintended consequences for the availability of future medicines.

Intellectual property has become established over centuries in countries as a solution to protect and provide incentive for creativity in a competitive market. Society has struck a bargain with those who invest to innovate to protect their new and inventive products for a period of time during which they can gain fair reward for their efforts. The originator gets the sole right over what they have patented for a set period of time – after this point anyone can make, use or sell. In practice, originators may manufacture the product themselves, grant a licence to other companies to manufacture the goods on their behalf or sell the patent outright.

In return, information on their scientific inventions and new manufacturing practices are made available to the whole world through publication. Applying for a patent means the originator has to put on full public record exactly what they have created, explain how it works and how it is made. The publication of patent information allows other research workers to develop their knowledge and push forward the boundaries of techniques in the science by using the published information to develop further responses to the same problem. In this way, patent publications do not prevent scientific enquiry and encourage further research into particular diseases.

There is no such thing as a 'world patent' and patents are only effective in countries where they are applied for and granted. The limited period of exclusivity granted by a patent gives the patentee time to try to make money from the invention to recoup the substantial cost of research and development and, importantly, generate funds for ongoing future R&D. With so many diseases yet to be fully understood, a strong pharmaceutical industry is vital to developing the medicines of tomorrow.

And this is the point: patents are a solution that has been evolved by society to balance the public interest with the power of competition to make important discoveries that benefit us all. Removing patents would make the world risk-averse to innovation and encourage corporate secrecy – neither are positive steps, especially for infectious diseases that constantly evolve to develop resistance to current drugs.

Intellectual Property in itself is not a barrier to access and delivers huge benefits to society both in terms of generating research for new medicines and in making

innovators fully accountable for these inventions; something that no system that relied on public investment or 'open source' science can achieve. Without encouraging innovation, there will be no new medicines – and this is a problem not just for tackling areas of unmet need, but for the many infectious diseases (e.g. malaria, tuberculosis) which build drug-resistance over time. The world needs well-resourced, research-based pharmaceutical companies because they fulfil a vital social need for new medicines – without these companies, health across the world would not merely stand still. It would start to fall back.

CASE STUDY 5: Sustainable low pricing and voluntary licensing

GlaxoSmithKline has offered sustainable preferential pricing for antiretrovirals (ARVs) since 1997. All its ARVs are now available at not-for-profit prices to public sector customers and not-for-profit organisations in all Least Developed Countries (LDCs) and all of sub-Saharan Africa – 64 countries in total. In addition, all private employers in sub-Saharan Africa who provide care and treatment to their uninsured staff can purchase its ARVs at not-for-profit prices. All Country Co-ordinated Mechanism (CCM) projects fully funded by the Global Fund to Fight AIDS, TB and Malaria and projects funded by the US President's Emergency Plan for AIDS Relief (PEPFAR) are also eligible.

GSK's prices are sustainable – it does not make a profit on them, but it does cover its costs. This means that it can sustain supply of these high-quality products for as long as they are needed. GSK's not-for-profit prices are applicable to orders of any size and are not dependent on large order quantities. They also include insurance and freight costs. In May 2006, GSK announced further reductions in the not-for-profit price of its Abacavir-containing ARVs and also added two new ARVs, Kivexa and Telzir – to its not-for-profit offer.

In 2006 GSK shipped 27 million tablets of not-for-profit Combivir and 59 million tablets of not-for-profit Epivir to the developing world compared with 45 million and 81 million tablets respectively in 2005. This decrease was expected and is primarily caused by more customers purchasing ARVs from generic manufacturers, including those licensed by GSK. In 2006, GSK licensees supplied more 120 million tablets of their versions of Epivir and Combivir to Africa – a positive indication that GSK's licensing policy is working.

Beyond patents – licensing, TRIPS and DOHA

Extreme poverty means that many things in developing countries cannot work in the same way as in richer countries. To balance the rightful protection patents give innovators, governments have included within patent law other systems to ensure monopoly rights are not abused. These include, in the last resort, the rights for government to insist, in cases of national emergency, that the patent holder allows others to make products to their patent specification.

In recent years, many more companies have brought in tiered or not-for-profit pricing to make their medicines affordable to poorer nations. Where companies do not have the capacity to deliver this, voluntary licensing to a generic manufacturer is another approach some companies are taking. Licensees get the benefit of advice and support from the originating company to ensure their version of the medicine is made to a high standard.

These approaches are favoured by the industry because they retain some control over the quality of their medicines, and they are better for countries because quality and effectiveness of the medicines are assured. They also bring wider benefits such as sustainability of reliable supply, the ability to scale-up production to meet patient need, transfer of high-technology to poorer nations and create local employment.

Under international trade agreements, countries have agreed between themselves that governments should have the final resort of a right to compulsory licensing of a medicine to provide an alternative supply of medicines in cases of national emergency. While already possible under UK patent law, until relatively recently this was not a part of many countries' laws. This harmonisation of patent laws around the world is part

of the WTO agreement on 'Trade Related Aspects of Intellectual Property Rights' (TRIPS).

Defining when it is appropriate to issue compulsory licences is the source of some controversy. Recent decisions to broaden the use of compulsory licensing in Thailand and Brazil, both middle-income countries with growing market economies alongside very stark social inequalities, raise questions about the stability of trade agreements, patents and the climate for innovation. Best results for patients can be achieved if nations negotiate with originating companies over affordable price and voluntary licensing schemes that ensure quality in the first instance, rather than risking reverse-engineering versions of medicines as anything but a last resort.

TRIPS & the Doha declaration

TRIPS is a short-hand term used to describe one aspect of the General Agreement on Tariffs and Trade (or GATT) made between World Trade Organisation (WTO) member nations. The initial TRIPS agreement was made at the Uruguay round of WTO negotiations and came into force in 1995.

The TRIPS agreement covers a wide range of subjects dealing with different aspects of trade around the world and aims to reduce:

> *"distortions and impediments to international trade, promotion of effective and adequate protection of IP rights and ensure that measures and procedures to protect IP rights do not themselves become barriers to legitimate trade".*

The initial TRIPS agreement only allowed countries to issue compulsory licences for medicines that could be manufactured in their country – of little use to the very poorest countries without high-tech manufacturing capacity. At the 2001 Doha round of WTO talks, ministers agreed a mandate for negotiations on the subject of how TRIPS might assist a number of emerging health crises in the developing world where member nations had no manufacturing capabilities.

After long discussions, the WTO agreed in August 2003 to pilot a temporary scheme allowing manufacturers to obtain compulsory licences to export their products into developing nations to extend emergency relief for pandemic disease. The agreement allows for a workable solution for compulsory licensing for export but maintains respect for intellectual property.

At the subsequent round of talks during 2005 in Hong Kong, WTO ministers agreed that this arrangement should now be made a permanent part of TRIPS. However, to date, only around seven out of 150 of the member nations have ratified the extension agreement within their national legislation.

The vital role of generic medicines manufacturers

Manufacturers of generic medicines have a vital role to play in tackling disease by providing older – but still effective medicines – at low prices once they go out of patent protection (or "off-patent"). As already stated, some 95% of the WHO's essential medicines are available off-patent and theoretically cheaply – but are still not reaching patients.

Generics companies can afford to provide medicines at low cost because they do not carry the huge costs and burdens of research and can simply focus on manufacture of the medicines themselves, which in itself is relatively inexpensive. Because of the great number of these companies, direct competition on price can be fierce and their existence provides the manufacturing capacity required to supply enough quantities of medicines to treat the world.

But what these companies cannot do is provide answers to problems of disease that remain unsolved, as they do not engage in research & development. They also operate under sharp market conditions which focus manufacturing efforts where there are greatest opportunities to undercut prices and cannot be guaranteed to provide long-term continuity of supply for life-saving medicines. It is important to remember that these are private companies operating on extremely tight profit margins and cannot always be

relied upon to produce essential medicines over the long-term. For example, in the area of TB, there are many old but still effective medicines which are complicated and expensive to manufacture and have therefore been neglected by generic manufacturers. As the original inventor of these medicines, Lilly has a project to encourage generic manufacturers to enter into production and help meet demand.

Generic medicines manufacturers rely on research-based branded medicines companies to sustain their business and so cannot be the sole answer to improving access to medicines in the developing world, even though they remain a vital part of the solution. In fact, in some developing countries patients are suspicious of generic medicines because of the high prevalence of low-quality counterfeits. It must be an important part of patient education to promote usage of high-quality generic medicines wherever they are available.

Research in the developing world

Neglected diseases

Aside from promoting access to medicines that already exist and the healthcare infrastructure to support it, pharmaceutical companies are putting research into neglected diseases and finding new ways to make formulations of existing medicines work better in developing world clinical settings. A wide range of companies are devoting research efforts to neglected tropical infectious diseases. Some work in partnership with academics on specific disease projects; others – notably GSK, Novartis, Pfizer and AstraZeneca – have set up dedicated research centres that specialise in the field.

CASE STUDY 6: Pfizer-WHO tropical disease partnership for drug discovery

Pfizer's collaboration with the WHO Special Programme for Research and Training in Tropical Diseases

(WHO/TDR), announced in October 2006, is part of a new effort to link the research resources of a major pharmaceutical company to a global network of discovery research. It will speed up the search for new drugs to combat some of the world's most deadly parasitic diseases, including malaria, leishmaniasis, African trypanosomiasis, onchocerciasis, schistosomiasis and Chagas disease.

As part of this collaboration, Pfizer gives access to its library of medicinal compounds – the world's largest – and also brings scientists from developing countries into Pfizer's laboratories for training in drug discovery techniques. Under the arrangement, scientists in institutes affiliated with the WHO/TDR-sponsored Compound Evaluation Network are testing thousands of compounds from the Pfizer library. In a process called screening, the researchers are seeking to identify hits – compounds that show initial activity against a range of tropical parasites.

Developing country researchers supported by a second WHO/TDR network – the Medicinal Chemistry Network – are working with scientists at Pfizer's laboratories in Sandwich, Kent further to evaluate the hits and from them select lead compounds – those with the greatest potential to be developed into new medicines for parasitic disease treatment and prevention. They are also being trained by Pfizer scientists in the latest drug discovery research methods and use of state-of-the-art tools. Following this training, they will return to their home countries to deploy their new knowledge and skills.

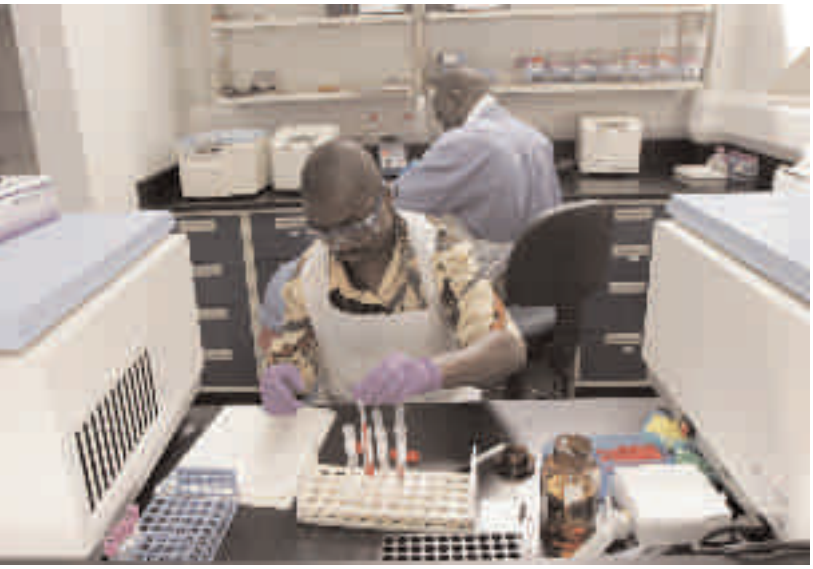
Pfizer has initially provided 12,000 compounds, many of which are known to have activity against protozoan or helminth parasites. As WHO/TDR increases screening capacity across its network, Pfizer will provide more compounds. The company's scientists will identify the compounds most likely to address biochemical targets associated with anti-parasitic activity.

Pfizer believes public-private research collaborations are vital to tackling health challenges in developing countries. The company is already exploring ways in which the collaboration with WHO/TDR might be expanded to aid further in the search for drugs with the potential to treat tropical diseases. Pfizer hopes the new collaboration will encourage other companies to join and expand the WHO/TDR Networks, and to explore further collaborations with developing country researchers in discovery research.

Some critics of pharmaceutical industry research priorities have often suggested that there exists a '10/90' gap in research for medicines. That is that 90% of research goes into diseases that affect just ten per cent of the world population. In fact, pharmaceutical research is very well aligned to the global disease burden with the focus firmly on the main killers. Even today, by far the biggest killer in high and low income countries is the same – coronary heart disease[xiv].

Patients in developing countries get cancer and heart disease just like their counterparts in richer nations – and if better access to healthcare means the simpler infectious diseases that are currently taking a huge toll in poorer nations are controlled, then access to care for these more chronic conditions will be the next big area of focus for global health.

Important though it is to tackle alarming tropical diseases such as leprosy, leishmaniasis and sleeping sickness, it is important to keep these conditions in perspective. Truly neglected diseases account for less than one per cent of mortality in poor countries – a disease burden that is dwarfed by respiratory infections and diarrhoeal diseases for which effective treatment is available cheaply from generic manufacturers but is still not getting to patients.



Infectious Diseases Institute, Specimen Accessioning/ Processing Lab, Kampala, Uganda.

CASE STUDY 7:
Targeting neglected diseases – lymphatic filariasis

The Global Alliance to Eliminate Lymphatic Filariasis (GAELF) was created to eliminate one of the world's leading causes of disability and disfigurement as a public health problem by the year 2020. An estimated 120 million people in at least 80 countries of the world are infected with lymphatic filarial parasites and one billion (20% of the world's population) are at risk of infection.

Initiated by the WHO and GlaxoSmithKline in 1998, the Global Alliance has evolved into a global partnership between international organisations in the public and private sectors, academia and NGOs working in partnership with ministries of health in tropical countries where lymphatic filariasis (LF) is endemic. Merck & Co Inc joined the Alliance, when it widened the scope of its Mectizan Donation Program to include LF in African countries where river blindness and LF co-exist.

The WHO currently recommends that lymphatic filariasis be prevented with a combination of albendazole (donated by GSK) with either Mectizan (donated by Merck) or DEC (purchased locally). Drug administration for people living in endemic areas is recommended once a year for at least five years to break the cycle of

A boy in Togo is measured and then takes the correct dose of medicines to stop the transmission of lymphatic filariasis.

transmission. In 2006, GSK donated 155 million treatments of albendazole to prevent transmission in at least 34 countries in Africa, America, the eastern Mediterranean, Mekong basin, the Indian sub-continent and the Pacific region. To date, GSK has donated 600 million treatments.

Over the 20-year life of the programme, GSK expects to donate up to 6 billion preventative albendazole treatments across the 80 endemic countries that are accepted into the programme by the WHO. Merck donated 48 million treatments of Mectizan to LF elimination programs in 11 African countries and Yemen in 2006. Merck and GSK have also provided financial grants to support partners in research programmes, coalition building, workshops and communications. WHO estimates that more than 100 million people – 30 million of whom are children – are already being protected from LF.

A patient suffering from lymphatic filariasis is taught how to manage her swollen legs

Developing new formulations

Finding treatments for neglected diseases is an important area for research – but companies are also looking into ways of making existing medicines more suitable for the reality of healthcare in developing countries. Many treatments require things like sophisticated diagnostics, close observation by highly skilled clinical staff or careful temperature control. All of these are available in well-developed health systems, but not in many developing countries. Paediatric formulations of medicines are a particular need in some therapeutic areas.

Clinical trials in developing countries

Discovering cures for diseases that affect developing countries or finding ways of using existing treatments that respond effectively to the infrastructure or cultural realities of developing world countries require clinical trials. Furthermore, clinical research into conditions that can only be found in the developing world can obviously only be carried out there.

Conducting such vital research in resource-poor settings represents practical difficulties, and sound ethical frameworks are vital to safeguard possible exploitation of research participants. Informed consent is the cornerstone of ethical clinical research and this becomes even more crucial in healthcare settings where participation in research might seem the only route to quality treatment.

Getting good ideas from the laboratory bench to patients safely is one of the most time-consuming and expensive parts of medicines development. Regulators like the UK Medicines and Healthcare products Regulation Agency (MHRA) or the US Federal Drugs Administration (FDA) rightly demand extremely high standards of proof before granting a medicine a licence. Some commentators have suggested that, for medicines designed for developing countries, a less rigorous and therefore cheaper level of regulation could be applied and possibly get medicines to patients more quickly and at lower cost. The pharmaceutical industry rejects this view as well-intentioned but dangerous – the highest standards must be maintained for all patients. In fact, pre-launch testing is even more important in developing countries because they do not have the failsafe systems of side-effect monitoring that are a key part of developed healthcare systems.

As in provision of healthcare and access to medicines, partnership with local governments and developing local research capacity is the way forward, to ensure both that research benefits the community that participates and that the use of the resulting innovation can be sustained.

Local organisations like the African Medical & Research Foundation (AMREF) and the INDEPTH Network are vital in building research capability and expertise in developing countries alongside strengthening community health infrastructure. If handled transparently, pharmaceutical research in developing countries is a vital engine in improving health infrastructure.

Disaster relief

Disasters, natural and man-made, create sudden and urgent emergency requirements for medical assistance both in dealing with injuries and the outbreaks of infectious disease that often follow. In the rush to support communities, it is vital that donated medical aid is of good quality, in-date and appropriate to need as well as supplied quickly.

These commitments are significant. For example, in the aftermath of the December 2004 tsunami, the global pharmaceutical industry donated medicines and cash to the value of more than £50 million. Most pharmaceutical companies have significant humanitarian programmes and donate substantial quantities of medicines each year.

In the UK, the ABPI works with a dedicated charity called International Health Partners (IHPUK). It acts as a clearing house to match requests for assistance from aid agencies and governments with relevant donating companies and manages the logistics of getting the medicines where they are needed. It has been active both in the tsunami and major earthquakes since.

GlaxoSmithKline has provided a fund for fishing communities to use to buy new boats, engines and nets, enabling them to re-establish their livelihood post tsunami.

Marketing health?

The dominance of science in how we understand and treat disease is so overwhelming in western developed nations that it is sometimes easy to forget that this is not necessarily the case in many areas of the world. Spiritual, shamanic or traditional healers, for example, hold great sway in many rural communities. Deeply held religious beliefs or political suspicions can also intervene – for example, in recent years, Nigerian imams called for a boycott of polio vaccination, believing it to be a US plot. In this environment, dangerous and tragic health myths can be spread. Social stigma can be a barrier for people to seek treatment.

Effective use of medicines and disease prevention requires concordance from an educated and convinced community. Many public sector organisations have lamented that they need to get better at "marketing health" and that lessons could be learnt from the private sector: one good example is promoting the uptake of mosquito bed nets and their regular replacement as the insecticide wears off. Many medicines must be taken for a full course or resistant-strains of disease will develop more quickly. There is a clear expertise and interest for the pharmaceutical industry to assist – but it is vitally important that any intervention in areas of the world where exposure to modern medicine is low is carried out ethically, transparently and sensitively.

CASE STUDY 8: Novartis and leprosy

Novartis has, through its Novartis Foundation for Sustainable Development, been a major partner in the WHO's strategy to eliminate leprosy. The company developed two out of three of the medicines in a multi-drug therapy (MDT) for the condition which offers cure, prevents transmission and prevents disability. Since 2000, Novartis has supplied MDT free for all patients in the world through the WHO and in coordination with its programme of education and diagnosis. Novartis has covered all costs of freight, insurance and independent quality control of these medicines and has committed to continue uninterrupted supply until 2010.

The Novartis foundation has backed the medicines donation by assisting governments, WHO and NGO field missions in pioneering social marketing in combating the disease. The underlying concepts of generating and meeting demand for leprosy treatment are now an integral part of the WHO leprosy elimination strategy. Novartis Foundation also helped simplify the provision of disability prevention services in communities.

The impact of the WHO programme has been the cure of 14 million people (4 million directly through the WHO-Novartis collaboration). The global prevalence rate has dropped by more than 90% since 1985 from 21 per 10,000 people to fewer than 1 and all but five countries in the world have eliminated leprosy. Detection of new cases has decreased by 20% per year for the past three years.

IFPMA code of practice

The global umbrella body for the pharmaceutical industry, the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) has a code of practice to maintain high ethical standards across the globe.

The code sets clear standards which state that the industry has an obligation and responsibility to provide accurate information and education about its products to healthcare providers in order to establish a clear understanding of the appropriate use of prescription medicines.

Promotional activities and marketing practices must be consistent with high ethical standards, and information should be designed to help healthcare providers improve services to patients. Information must be provided with objectivity, truthfulness and in good taste, and must conform to all relevant laws and regulations. Claims for therapeutic indications and conditions of use must be based on valid scientific evidence and include clear statements with respect to side effects, contra-indications, and precautions.

High standards of ethical behaviour must apply equally to marketing of pharmaceutical products in all countries, regardless of the level of development of their economic and healthcare systems. This is vital if the contribution of modern pharmaceuticals to world health is to be trusted and embraced.

The future and call to action

This publication has laid out some of the challenges, but also demonstrated some of the imaginative and innovative ways in which pharmaceutical companies are trying to meet these challenges of health in the developing world. But adequate quality healthcare remains out of reach for too many global citizens – much more needs to be done.

Today there is new hope and expectation that a concerted effort from governments, international organisations, voluntary and private sectors in rich and poor countries can bring further steps forward for health in developing countries. This has come about because of a growing awareness that private and public sector share the goal of improving health and have been able to find common ground, and because developed world governments have made substantial financial commitments.

However, the interlinking issues of poverty and health are so complicated that they defy any attempts at easy resolution. Pharmaceutical companies have a big role to play – but there are limits to what they can realistically achieve alone. Here are some of the steps that can contribute to further advance:

Extending access through partnership – Solutions will be found by listening to local communities, empowering local leadership and development, carefully targeting aid and by seeking consensus across a wide range of organisations and ideological perspectives. These growing partnerships are vital to our success.

Sensitive pricing and licensing – For medicines that are in patent, an increased use of tiered or not-for-profit pricing and voluntary licensing can ensure more affordable supplies of quality-assured medicines.

Maintaining global innovation through intellectual property rights – The stable structure to world markets and trade that patents provide is absolutely crucial to sustaining the massive investment in research and development still required to find new treatments for unmet health needs. It remains unlikely that any publicly funded mechanism could realistically fill the gap if incentives for research-based pharmaceutical companies were removed.

Sustainability and planning for the long-term – Sporadic medicines donations cannot be guaranteed in the long term and risk leaving communities worse off than before. Measures that build local health capacity and can be self-perpetuating must be the prime aim of intervention from rich nations. Much more needs to be done to spread best practice between developing countries to address local needs, as this is far more effective than forcing top-down approaches from richer nations.

Avoiding 'market failure' to address need – Where local markets are so limited they cannot drive innovation, then other economic machinery (for example, advanced market commitments from richer nations) must be used intelligently and efficiently to encourage private industry to provide solutions.

Fighting corruption and trade tariffs – Stronger institutions and a long-term view on import duties, taxes and unjustified mark-ups within developing countries would reduce costs of medicines, combat dangerous counterfeits and help promote wider access. It is vital to police illegal trade in counterfeits and stop profiteers from exporting low-price goods away from the countries where they were intended to be used. If profiteers are able to import reduced price products back to the developed world to be sold cut-price on the very markets where the manufacturer needs to make a profit, this undermines lower prices in developing world countries – so destabilising both the economic balance and the supply chain to the developing world.

Plan for long-term success – Solving the current crisis in infectious diseases will be a hollow victory if we then fail to plan for coping with conditions like cancer or heart disease. We need to develop holistic long-term solutions for developing world health systems.

Mobilising all of industry – All private industry working in developing countries has a role to play in improving health. All industry could play a wider role in partnerships - either through supporting the health of their employees, facilitating health education or by bringing their technical expertise to bear on issues like basic infrastructure.

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For more information about the ABPI and its related organisations, visit our websites:

ABPI
www.abpi.org.uk

Office of Health Economics
www.ohe.org

Prescription Medicines Code of Practice Authority
www.pmcpa.org.uk

Electronic Medicines Compendium
www.medicines.org.uk

Information about careers in the pharmaceutical industry
www.abpi-careers.org.uk

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