



Tackling the diseases of poverty

**Meeting the Okinawa/Millennium targets for
HIV/AIDS, tuberculosis, and malaria**



**Performance and Innovation Unit, Cabinet
Office, London.**

8 May 2001

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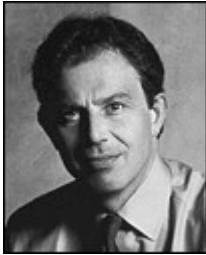
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PIU working papers

These papers will be published independently of this report on the PIU website. The address of our website is: <http://www.cabinet-office.gov.uk/innovation/>

- Working Paper 1: The situation and existing action to tackle HIV/AIDS, TB and malaria
- Working Paper 2: The rationale for government intervention
- Working Paper 3: Innovative solutions for fundraising
- Working Paper 4: Innovative solutions for tackling these diseases

Foreword by the Prime Minister



The developing world now faces a health crisis on an appalling scale. Three diseases - HIV/AIDS, TB and malaria - kill around 5.4 million people a year and debilitate around 250 million sufferers. The economic and social consequences for the poorest countries are devastating, and threaten to reverse decades of development.

That was why the leaders of the G8 countries committed themselves last year to work in partnership to achieve by 2010 substantial reductions in the burden of death and disease associated with HIV/AIDS, TB and malaria.

The only way to achieve such reductions is through a truly a comprehensive strategy. Health systems need to be improved and expanded, health promotion scaled-up. Vaccines, drugs and other health products to prevent and treat the diseases need to be made available to those who need them at a price they can afford. And new, more effective health products need to be developed to overcome drug-resistant disease strains and offer alternative methods of prevention.

I asked the Performance and Innovation Unit to report on the policy options which could be adopted by the international community to lift the burden of disease shouldered by the world's poorest. I am grateful to Stephen Timms MP, Financial Secretary to the Treasury, for overseeing work on this project as its Sponsor Minister.

The Government is publishing this report as a contribution to the international debate rather than a statement of government policy. It proposes actions that national governments and the international community can take to improve health care systems and health promotion; to make existing health products more affordable, and to provide incentives for additional research into new, more effective health products.

The message of this report is clear. We face a truly global crisis. It needs a truly global response. That means bringing together governments, civil society and the private sector in developed and developing countries, multilateral agencies, and international financial institutions.

The UK is committed to playing its part in a much larger and better co-ordinated international effort to tackle communicable diseases in the developing world. At the *International Action Against Child Poverty – Meeting the 2015 Targets* Conference in London in February 2001, the UK Chancellor and Secretary of State for International Development outlined a series of measures to address the devastation caused by HIV/AIDS, TB and malaria, including a global fund, tax relief for product donations, and tax incentives for research and development of

new products. At the Spring Meetings of the IMF/World Bank in April 2001, the Chancellor and other G7 finance ministers put their support behind a new initiative to tackle these diseases.

We want to maintain the momentum that is already building up. The world faces an unprecedented health challenge. We need to be prepared to act decisively – and in partnership - to tackle it before it's too late.

Tony Blair

Executive summary

The problem ...

- 1 1.2 billion people – a fifth of the world’s population - survive on less than \$1 a day. The degree of poverty that persists is accompanied by the spread of instability, conflict, population displacement, environmental degradation and disease.
- 2 To help bring a focus to efforts to eliminate poverty, the international community has signed up to an ambitious set of international development targets which cover economic well-being, social and human development (education and health), and environmental sustainability and regeneration. The UK is strongly committed to mobilising a stronger international effort to meet these targets.
- 3 Health is fundamental to economic growth and poverty reduction, and *vice versa*. The developing world faces a health crisis that threatens to reverse the development gains of the last 50 years. Three communicable diseases - HIV/AIDS, tuberculosis (TB) and malaria - kill around 5.4 million people a year and debilitate around 250 million sufferers in developing countries.
- 4 The social and economic consequences of HIV/AIDS, TB and malaria for the poorest countries are devastating. By 2010, it is estimated that 17 million children in Africa will be orphaned by HIV/AIDS each year. Ending the HIV/AIDS epidemic might translate into 1.5-4.5 percent higher GDP per capita growth in Sub-Saharan Africa. A 50 percent reduction in the burden of malaria might translate into a 1.5 percent increase in GDP per capita growth in those countries most affected by the disease.
- 5 Health care delivery systems in developing countries are often inadequate to ensure that advice and treatment is available to those who need them. Efforts to tackle HIV/AIDS, TB and malaria are often not integrated into national health systems and delivered through vertical programmes, which divert human and financial resources and undermine weak systems.
- 6 Effort is also needed to ensure that the health products required to tackle HIV/AIDS, TB and malaria - vaccines, treatment drugs, and non-pharmaceutical products such as condoms and bednets - are both effective and affordable.
- 7 Existing health products to tackle HIV/AIDS, TB and malaria are not only unaffordable to those who need them, but many are increasingly ineffective. Widespread failure to complete complex and lengthy treatment programmes has led to a rise of multi-drug resistant TB. Mutating strains of malaria render existing drug treatments ineffective.

The challenge ...

- 8 Major communicable diseases like HIV/AIDS, TB and malaria do not respect geographical or political boundaries. It is therefore in everyone’s interest to help to tackle these diseases.

- 9 There is already substantial action underway to tackle HIV/AIDS, TB and malaria. However, both analysis of gaps in global activity and estimates of the annual shortfall in resources available to tackle these diseases suggest that more action is required if a devastating health crisis is to be avoided.
- 10 This shortfall in efforts was recognised by G8 leaders at the Okinawa Summit in July 2000 where they committed to work in partnership to achieve by 2010:
- a 25 per cent reduction in HIV/AIDS among people aged 25 years or younger;
 - a 50 per cent reduction in prevalence and deaths from TB; and
 - a 50 per cent reduction in the burden of disease associated with malaria.

The way forward ...

- 11 In order to meet these targets, a global strategy is needed which can be adopted by the international community. This report sets out a possible package of measures and options for consideration by the international community, focusing on measures to improve the affordability and effectiveness of products needed to combat HIV/AIDS, TB and malaria.
- 12 In November 2000, UK Prime Minister Tony Blair pledged that the UK Government would investigate ways of achieving better availability of health products to prevent and to treat HIV/AIDS, TB, and malaria in developing countries, to contribute to the achievement of 2010 targets.
- 13 Achieving the targets requires a comprehensive global strategy which builds on and develops existing initiatives. A strategy to tackle the diseases needs to:
- improve and expand coverage of health care systems and health promotion;
 - help to increase access to existing health products in developing countries (where affordability is a key component of access);
 - improve incentives for additional research into new, more effective products; and
 - develop a more effective partnership to harness the expertise of governments and the private and voluntary sectors to combat these diseases in developing countries.
- 14 In February 2001, the UK Chancellor and Secretary of State for International Development announced UK support in principle for a Global Fund for Health. The Chancellor also announced new tax measures, further details of which were set out in the Budget in March 2001. At the IMF/World Bank Spring Meetings in April 2001, G7 Finance Ministers and members of the International Monetary and Financial Committee endorsed calls for an international response. The Chancellor and Secretary of State for International Development subsequently met the UN Secretary-General to encourage broad support.
- 15 This report to the UK Government is being published now to contribute to global policy discussions, inside and outside government, on how a global strategy should be put in place. It looks at the need to build on existing

initiatives to strengthen action on prevention and treatment and health care systems. But it has a particular focus on identifying policy measures required to address the issues of the affordability of health products and incentives to develop and supply them; and the need for partnership to deliver solutions in these areas.

Conclusions ...

- 16 This report concludes that a global strategy, based on an holistic approach to the issues, is required to meet the international targets. It identifies a need to scale-up efforts to strengthen action for prevention and treatment and health care systems. Using analysis undertaken for this report it then builds a package of policy measures to develop and supply effective health products at an affordable price, each of which targets an identified specific gap in current activity. The measures proposed have been assessed as offering the best prospect of securing large, rapid and sustained reductions in the disease burden facing the world's poorest.
- 17 The key components of the package for consideration by the international community include:
- additional support to improve **health care systems and health promotion** by donor governments and multilateral agencies (para 58);
 - a **new Global Fund for Health** to finance the purchase of existing products to tackle the three diseases, substantially scaling up the provision of these products to those most in need but least able to afford them (para 95);
 - an **advance purchase commitment** – a binding promise to purchase new, substantially more effective products as they become available, strengthening incentives to step up investment in research and development (para 99);
 - clarification of the flexibilities in intellectual property protection under the WTO TRIPS agreement, through global discussion on the terms under which they can be used; more widespread and more effective use of voluntary licensing agreements to allow local production; and a framework for tiered pricing of patented products. This will help to ensure that existing products are more affordable while also maintaining the incentives required for increased research and development investment to produce more effective products, through a joint commitment from governments, industry and civil society (para 105);
 - tax credits for R&D, a clinical trials platform and harmonisation of regulations, targeted financial support and public-private partnerships to stimulate, and remove blockages to, basic and applied research (para 130); and
 - a **scaled-up and better co-ordinated global partnership to halt and reverse the spread of disease**, including substantial additional resources and commitment to more effective ways of working together from governments, civil society and the private sector in developed and

developing countries, multilateral institutions, the pharmaceutical industry, and international financial institutions (para 152).

18 It will require a substantial and sustained increase in financial commitment to tackle these diseases effectively. Developing countries' delivery systems are often weak and may not be able to absorb a rapid increase in resources and newly-affordable products. It is recommended that an incremental approach is taken, starting with a small but significant Global Fund for Health that can be scaled up over time to finance provision of effective health products. The best estimates from an analysis undertaken for this report show that such a fund could go some way towards meeting the Okinawa/Millennium targets.

19 For example, a Global Fund for Health of \$30 billion made up of a current fund of \$1 billion to be paid annually for 20 years, sustained in real terms, and an advance purchase commitment of \$10 billion to be paid as new products become available, could achieve:

- between 45 and 110 per cent (90 per cent central estimate) of the target for HIV/AIDS;
- between 55 and 110 per cent (90 per cent central estimate) of the target for malaria; and
- between 35 and 105 per cent (80 percent central estimate) of the target for TB.

A complete analysis of the proposed Global Fund for Health is included at Annex 2.

20 The challenge is immense and requires resources, expertise and commitment on a global scale. All members of the international community have a part to play and need to participate fully in this shared agenda.

21 The time to act is now.

The UK is actively engaged in discussions on these key areas with our international partners. We would welcome comments on the proposals contained in this report, which should be addressed to

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Key recommendations

- 1 Together with developing country governments, private sector and non-governmental partners, additional efforts are needed by developed country governments and multilateral institutions to scale up assistance to the health sector.
- 2 The international community needs to take action that:
 - significantly scales up resources to purchase effective health products that those most in need cannot afford;
 - establishes strong incentives for extra investment in research and development to accelerate progress towards the development of new vaccines, drugs and other products for these diseases;
 - strengthens support for basic research;
 - addresses blockages at the clinical trials stage of pharmaceutical product development;
 - reduces delays caused by variations in national product regulation; and
 - improves co-ordination between existing initiatives.
- 3 A Global Fund for Health should be established to purchase existing effective products to tackle the diseases, and include an advance purchase commitment to buy new, more effective products as they come onto the market. This will serve the dual purpose of:
 - providing an effective mechanism for financing the provision of health products to the poorest in developing countries; and
 - ensuring that incentives are sufficient to secure the substantial increase in investment in research and development of new products needed to make substantial, rapid inroads into the disease burden in the future.
- 4 An international advance purchase commitment should be established as an integral part of the Global Fund for Health. In particular, it is important that national governments consider creatively how best to establish a credible long-term commitment within existing budgeting frameworks, while ensuring that effective financial control is maintained.
- 5 There is a strong case for the WTO TRIPS Council to seek to clarify the flexibilities, including terms which allow use of compulsory licensing, available within the WTO TRIPS Agreement to help WTO members in achieving the Okinawa/Millennium targets. This should involve consultation with a working group of developed and developing country governments, the private sector, and relevant multilateral and non-governmental organisations.
- 6 We propose that this working group also considers ways in which voluntary licensing agreements between the pharmaceutical industry and developing countries can be made more widespread and more effective as a means of improving the affordability of health products for the poorest.
- 7 We propose that the international community should support a system of tiered pricing by putting in place a facilitative framework to ensure that low

prices can be charged to the poor - without low-priced products being re-imported to higher price markets. This requires action both by producers – for example recognisable differential packaging – and by governments to ensure simple and effective trade regulation to prevent parallel importation. It also requires political will in developed countries, to accept that the poor in developing countries should pay less than home markets, and also in developing countries, to ensure low price products reach the poorest and are not sold on to higher price markets.

- 8 We suggest carefully targeted public support for basic and applied research should be established, including innovative public-private partnerships to leverage private funds and expertise. We support harmonisation of regulations to speed up approval and licensing of new, more effective products.
- 9 To maintain an appropriate focus for additional public support for R&D, additional funds should, in the first instance, be restricted to activities related to new products to tackle HIV/AIDS, TB and malaria. This restriction should be subject to periodic review, with a view to later inclusion of research on products to tackle other diseases whose burden falls predominantly on the world's poorest people.
- 10 Products eligible for support should include vaccines, diagnostics and drug treatments, other – as yet unknown – products and significant improvements to the efficacy of existing products.
- 11 Public-private partnerships should be considered as a useful channel for additional public support, subject to appropriate governance and accountability structures, and the monitoring of progress and outputs. Rationalisation of the proliferation of existing initiatives should be encouraged.
- 12 We recommend that following the UK announcement of tax-credits for R&D, other developed country governments should consider adopting similar national tax measures to strengthen incentives for R&D in these diseases.
- 13 There is a strong case for the establishment of a clinical trials platform along the lines proposed by the EC, subject to agreement that developing countries would play a leading role in its development and operation; that trials would be restricted to products to tackle diseases of poverty in developing countries, with initial priority given to HIV/AIDS, TB and malaria. Access should be open to all appropriate products, without discrimination by global location or sector but with application of suitable user fees. It is important that work to establish a clinical trials platform – EC led or otherwise – begins soon, so that new products emerging in the near future can be appropriately trialled without delay.
- 14 We suggest appropriate human and financial resources should be set aside to speed-up product approval by regulatory bodies in developed and developing countries, and harmonise the requirements imposed by developing countries.

The role of the PIU

The creation of the Performance and Innovation Unit (PIU) was announced by the Prime Minister on 28 July 1998 as part of changes following a review of the effectiveness of the centre of Government by the Cabinet Secretary, Sir Richard Wilson. The PIU's aim is to improve the capacity of Government to address strategic, cross-cutting issues and promote innovation in the development of policy and in the delivery of Government's objectives. The PIU is part of the drive for better, more joined-up government, tackling issues that cross public sector institutional boundaries on a project basis. The unit reports directly to the Prime Minister through the Cabinet Secretary.

Comprehensive information about the PIU and its projects can be found on the PIU's website at www.cabinet-office.gov.uk/innovation

Sponsor Minister, Project Team and Consultants

The **sponsor Minister** for this project was Stephen Timms MP, Financial Secretary to the Treasury.

The **project team** consisted of the following:

Joanna Brown	PIU
Sarah Dearing	PIU
Daniel Instone	Seconded from the Department of the Environment, Transport and the Regions.
Alison Kilburn	PIU
Tracey Lane (deputy team leader)	Seconded from the Department for International Development.
Richard Price (team leader)	PIU
Jamie Rentoul	Deputy Director, PIU
Ruth Shinoda	Seconded from the Department of Health.
Howard Taylor	Seconded from the Department for International Development.
Shane Tomlinson	PIU

Consultants to the project team provided expert input on a part-time basis during the course of the analysis. The project team itself is responsible for the report's findings and final recommendations.

Andy Francis	Brookings Institution, Washington D.C.
Fabià Gumbau	Department of Economics, Harvard University
Julia King	Director of Corporate Policy, GlaxoSmithKline

Michael Kremer	Professor of Economics, Harvard University, and Senior Fellow, Brookings Institution, Washington D.C.
Ben Olken	Department of Economics, Harvard University
Jonathan Portes	Independent Consultant to the PIU
Patrick Vaughan	Emeritus Professor of Public Health & Epidemiology, London School of Hygiene & Tropical Medicine

Consultees and others

The team worked closely with others at HM Treasury, the Department for International Development, the PIU, and UK overseas embassies, missions and delegations during the course of the project. We consulted a large number of individuals and organisations – listed at the end of this report - who helped us to develop the analysis used in this report.

We are very grateful for the time and assistance they provided. Naturally, they have no responsibility for the opinions expressed in this report, nor for any factual errors or omissions. We apologise to anyone who has been inadvertently omitted.

Introduction

Background and aims

- 1 On 8th November 2000 the UK Prime Minister Tony Blair announced that the Performance and Innovation Unit would undertake a project examining:
“how to achieve better availability of drugs to prevent and treat HIV/AIDS, tuberculosis and malaria in developing countries and help achieve the targets for these diseases agreed at the G8 Okinawa summit”⁺
- 2 This report to the Government sets out the analysis, findings and recommendations of this project. The project team worked closely with the UK’s Department for International Development and HM Treasury, the UK finance ministry, in developing its proposals; as well as consulting a wide range of parties world-wide.
- 3 The project recognises that a huge amount of existing effort is already underway world-wide and that a wide range of discussions on new policy measures is required to tackle the health crisis. This report is intended to inform these policy discussions and to allow a wide range of individuals and organisations to respond to its proposals.
- 4 The report examines the need to build on existing initiatives to strengthen preventative and treatment action and health care systems. But it has a particular focus on identifying policy measures required to address the issues of affordability and incentives, and the need for partnership to deliver solutions in these areas.

Understanding the problem (Chapters 1 to 4)

- 5 To establish a sound basis from which to identify appropriate and effective policy measures, the project examined:
 - the causes, prevalence, incidence and impacts of these three diseases;
 - the scale and effectiveness of current activity and the barriers preventing the diseases from being tackled, and
 - the current state of development of existing and potential new products to tackle the diseases (including drugs, vaccines and other products such as insecticides), assessing their effectiveness and cost-effectiveness, and for products currently in research and development, their likely “time to market”.
- 6 The analysis of the scale and effectiveness of activity to tackle the disease burden (Chapter 3) identifies areas where necessary activities are “missing”, and the gap between the current scale of activity and what would be needed to achieve substantial, lasting reductions in the disease burden. It also considers the underlying causes of the shortfall in effort, including market failures and the poverty of those most at risk, that policy interventions need to address.

⁺ The targets adopted by the G8 Governments at Okinawa, and the G8’s commitment to take action, are set out in the G8 Okinawa Summit Communiqué, attached at Annex 1.

Developing the proposals (Chapters 5 to 7)

- 7 Chapter 5 sets out the approach used to identify a set of policy measures offering the best prospect of achieving reductions in the disease burden, for consideration by the international community.
- 8 The proposals in this report have been developed:
- on the best current understanding of the diseases, their impacts, and possible interventions to tackle them;
 - recognising that robust and effective national health strategies in developing countries are a prerequisite for improving health outcomes;
 - considering the efficacy, cost-effectiveness and affordability of both existing and potential new health interventions, and the speed with which they are likely to become available; and
 - to operate on a global scale, focussing on achieving substantial gains in health outcomes in developing countries, and to establish a partnership of players in developed and developing countries, inside and outside government to forge a new commitment to tackling communicable diseases of the poorest.
- 9 Drugs and vaccines are an essential component of a health care system, but they are only one part. Measures which tackle the affordability of health products and incentives to develop and supply them need to be set firmly in the context of action to improve developing countries' healthcare systems. Developing country governments need to take the lead in determining how best to upgrade systems and to expand their coverage. The developed world must provide support, resources, practical help and training where it is needed.
- 10 In consultation with a wide range of parties working in the field – including governments, multilateral agencies, pharmaceutical and bio-pharmaceutical companies, researchers, academics, private donors and non-governmental organisations* - we identified a wide range of possible policy interventions which might be used to correct for the gaps in and barriers to current activity to tackle the disease burden. Measures were assessed against a number of criteria to establish their likely contribution to a package that could be adopted by the international community.+
- 11 In particular, measures were assessed on their likely effectiveness against each of the diseases; their cost and cost-effectiveness; the likelihood that they will contribute to rapid reductions in the disease burden; and their ease of implementation. Substantial new analytical work was undertaken for the PIU by a team based at the Brookings Institution, Washington D.C. The work was used by the PIU and Brookings to assess the cost and health impacts of a range of measures on affordability and take-up of existing products to tackle the diseases, and on incentives to invest in and to accelerate research and

* A list of parties consulted can be found in the Annex.

+ The criteria, and the role of each proposed policy measure in correcting for a gap or barrier to action, are set out in Chapter 5.

development activity to produce substantially more effective/cost-effective products. This work has been used to underpin the analysis of policy options and recommendations.^Φ

A global strategy and specific measures

- 12 Chapter 5 concludes by showing how each component of the package contributes to tackling the disease burden by correcting for the barriers to activity identified in the report. Each component makes a distinctive contribution, complementing the effectiveness of the package as a whole.
- 13 Chapters 6 and 7 then consider the specific policy measures in more detail, setting out both a recommended way forward, and in several cases key choices on such matters as implementation and governance which will need to be made by the international community.

A call to action

- 14 Chapter 8 draws together our recommendations and key points on which decisions are required. It calls for substantial new effort from a global partnership of developed and developing country governments, multilateral agencies, the private, voluntary and academic sectors, researchers and private foundations. Nothing less will be sufficient to tackle and reverse the health crisis facing the world's poorest.

^Φ Annex 6 summarises this analysis.

Chapter 1: Poverty and health

Summary

- 1.2 billion people survive on less than \$1 a day. There is both a moral obligation on the international community to eliminate poverty, and an acknowledged self-interest in doing so.
- The instability, conflict, population displacement, environmental degradation and disease that accompany poverty do not respect national boundaries.
- Improved health is fundamental to economic growth and poverty reduction, and *vice versa*.
- The economic gains of good health are relatively greater for those poor people who are hardest hit by ill health.

1.1 It is in all our interests to end poverty ...

- 15 1.2 billion people – a fifth of the world’s population – live in extreme poverty, surviving on less than \$1 a day. They lack opportunities and services. They feel isolated and powerless and are often excluded by ethnicity, caste, geography, gender or disability. They also lack health information, access to health and education facilities, and to productive assets or to the market for their goods or labour.
- 16 Eliminating poverty is the biggest moral challenge facing the world today. It is in all our interests to succeed in the challenge. The degree of poverty that persists is accompanied by the spread of instability, conflict, displaced population, environmental degradation and disease, none of which respect geographical or political boundaries. Poverty elimination is possible within a generation, however, there is no guarantee that it will be achieved.
- 17 This report explores the most cost-effective ways to improve international action to tackle three particular communicable diseases - HIV/AIDS, TB and malaria - that threaten to reverse the development gains of the last fifty years.

International targets

- 18 At a series of UN conferences throughout the 1990s, the entire UN membership agreed a set of ambitious international development targets to focus efforts and measure progress in poverty reduction (see Box 1.1). The targets - also known as the 2015 targets - cover economic well-being, social and human development (education and health), and environmental sustainability and regeneration. Qualitative targets cover democratic accountability, the protection of human rights and the rule of law.

Box 1.1 International Development Targets

- A reduction by one half in the proportion of people living in extreme poverty by 2015.
- Universal primary education in all countries by 2015.
- Demonstrated progress towards gender equality and the empowerment of women by eliminating gender disparity in primary and secondary education by 2005.
- A reduction by two-thirds in the mortality rates for infants and children under age 5 by 2015.
- A reduction by three-fourths in maternal mortality by 2015.
- Access through the primary healthcare system to reproductive health services for all individuals of appropriate ages as soon as possible, and no later than the year 2015.
- The implementation of national strategies for sustainable development in all countries by 2005, so as to ensure that current trends in the loss of environmental resources are effectively reversed at both global and national levels by 2015.

- 19 International commitment to meeting the targets was strengthened at the United Nations Millennium Assembly in 2000. Nearly all the world's governments attended the Millennium Assembly and endorsed the targets. Progress towards the targets is also firmly on the agenda of G8 leaders, as confirmed at the G8 meeting in Okinawa in 2000 (see Box 1.2).

Box 1.2 Okinawa targets for health

- Reduce the number of HIV/AIDS-infected young people by 25% by 2010 (UN Secretary-General Report to the General Assembly on 27/3/2000)
- Reduce TB deaths and prevalence of the disease by 50% by 2010 (WHO Stop TB Initiative)
- Reduce the burden of disease associated with malaria by 50% by 2010 (WHO Roll Back Malaria)

1.2 ... and the UK is playing a major role ...

- 20 The recent White Paper on International Development reaffirms the UK's commitment to work to mobilise a stronger international effort to meet these international development targets. The UK played a leading part in securing enhanced debt relief for the poorest countries and at the end of 2000, twenty-two countries had begun to benefit from enhanced debt relief. Through support for the design and implementation of poverty reduction strategies, the UK Department for International Development (DFID) works closely with many governments to ensure that debt relief is translated into real improvements in the lives of the poor.
- 21 As part of the UK commitment to mobilise international support, at the *International Action Against Child Poverty – Meeting the 2015 Targets* Conference in London in early 2001, the UK Chancellor and Secretary of State for International Development challenged representatives of developed and developing countries, government and business, NGOs and civil society, UN agencies, the World Bank and IMF to set out how their respective institutions

planned to contribute to the global effort to eliminate child poverty and achieve the international development targets.

1.3 ... in breaking the vicious circle ...

- 22 Improving health is fundamental to economic growth and poverty reduction, and *vice versa*. At the household level, better health means less time and expense invested in caring for ill family members, improved physical and intellectual development, increased school attendance and learning, and higher productivity at work.
- 23 At the macro level, human development, and the demographic transition from high fertility and mortality to low fertility and mortality that is its consequence, is now widely accepted as a central long-term driver of economic growth. Economic gains of good health are relatively greater for poor people, who are the hardest hit by ill health.

1.4 ... but more needs to be done

- 24 There is no single determinant of good health. Education, the environment and access to health care services are particularly important determinants of health, and are all related to economic security. Age and sex are important, as are lifestyle, nutrition, social and community networks, living and working conditions, and broader socio-economic, cultural and environmental conditions. The determinants are inter-related and tend to move together to exert a combined influence on health.

Education

- 25 Improved education is a prerequisite for wider development and contributes significantly to better health. It enhances peoples' capacity to care for their own health and that of their families, and to make more effective use of health services.
- 26 Educating girls is particularly important to improve health; educated women are more likely to choose to have smaller, healthier families, to know when to use available health services, and to use them effectively. Even in the absence of community health programmes and facilities, educated women and their families fare better because they are better informed of the importance of personal health care and hygiene.
- 27 At the Dakar 2000 World Education Forum, the international community reaffirmed its commitment to the international development targets for education and Education for All. The UK supports the Dakar Framework of Action to achieve this commitments.

Nutrition

- 28 Adequate nutrition is essential for good health. Poor people tend to consume less protein and energy than necessary to maintain good health. What food they do eat often fails to provide a balanced diet, typically lacking sufficient key micronutrients, including iodine, vitamin A and iron. Nutritional deficiency adversely affects the immune system and reduces resistance to infection. Directly, or in combination with infectious diseases, inadequate diets

contribute to a large share of the global disease burden. The UK supports the work of UN agencies, including the Food and Agricultural Organisation, the World Food Programme, and the World Health Organisation, who work in partnership with others across the world towards food security and food safety for all.

Environment

- 29 Environmental factors, particularly indoor and outdoor pollution and lack of access to clean water and sanitation, are responsible for almost a quarter of all disease in developing countries. Poor households tend to live in a domestic environment that poses high health risk from an inadequate supply of potable water; poor sanitation; inadequate garbage disposal and drainage; poor ventilation and indoor air pollution; and overcrowding. The health risk from a poor domestic environment is compounded for many poor people by a poor working environment.
- 30 Many women and girls work in the home and suffer disproportionately from domestic health risks. Men, women and children from poor households also suffer from preventable injuries and deaths in high-risk occupations, and from chronic illness stemming from exposure to toxic chemicals, noise, stress, and physically debilitating work. Development agencies provide technical assistance and finance to developing country governments to promote consistent approaches to the environment across different government ministries, implement environmental improvements, and enforce environmental laws and regulations.

Public health services

- 31 Health services interact with households in two fundamentally different ways. Public health programmes tackle health problems of entire populations or population sub-groups. Their objective is to prevent disease or injury and to provide information on self-cure and on the importance of seeking health care. Public health programmes deliver specific health services, for example immunisation; and promote healthy behaviour and healthy environments.
- 32 Clinical services respond to demand from individuals and are provided by the public and private sectors. They generally seek to cure or ease the pain of those already sick. In developing countries, the private sector plays a large role in the provision of these health services.
- 33 Development agencies provide technical assistance and finance to developing country governments for public health programmes and to devise and implement health sector strategies aimed at ensuring everyone - particularly the poor – has access to an appropriate minimum level of health services.

Chapter 2: A health crisis in the developing world

Summary

- Communicable diseases remain the biggest killer and cause of ill health among the poor of the world and threaten to reverse decades of development gains.
- Three communicable diseases - HIV/AIDS, TB and malaria - kill over 5 million people a year in developing countries – with devastating social and economic consequences.
- The social and economic benefits from reducing HIV/AIDS, TB and malaria, coupled with the lack of an effective market for appropriate health products, warrants government intervention.

2.1 We must tackle communicable diseases ...

- 34 The global pattern of disease varies significantly between developed and developing countries. Non-communicable diseases, including cardio-vascular disease, mental illness and cancers, and injuries account for the majority of the disease burden in developed countries. Communicable diseases and maternal, perinatal and nutrition-related conditions account for the majority of ill health in developing countries. As countries develop and communicable diseases are brought under control, non-communicable diseases become the biggest cause of ill health.
- 35 Globally, an estimated 17 million people die every year from communicable diseases. Among the poorest fifth of the world's population - those who survive on less than one dollar a day - communicable diseases remain the biggest killer and cause of ill health. They are responsible for 59 per cent of deaths and 64 per cent of disability-adjusted life years (DALYs)⁺ lost. Among the richest one fifth of the world's population, the figures are 8 per cent and 11 per cent, respectively.
- 36 Tackling communicable diseases is a health priority for developing countries, and is essential if the international development targets are to be achieved. It is in the interest of everyone to help defeat the major communicable diseases prevalent in developing countries, as they do not respect geographical or political borders. Globalisation and more international trade and travel have increased the opportunities for cross-border transmission of disease. Global warming is predicted to increase the number of malaria endemic countries.

2.2 ... in order to lift the burden of disease ...

- 37 The developing world faces a major health crisis that threatens to reverse decades of development gains. Three diseases, HIV/AIDS, TB and malaria - kill around 5.4 million people a year in developing countries, more than a third

⁺ DALY: A unit used for measuring both the global burden of disease and the effectiveness of health interventions, as indicated by reductions in the disease burden. See the Glossary of Terms for more detail.

of their annual death toll. This is equivalent to a capacity crowd in an Olympic Stadium dying each and every week of the year. Chart 2.1 illustrates the regional pattern of deaths from HIV/AIDS, TB, and malaria.

- 38 Average life expectancy at birth in many developing countries world is less than 50 years; the developed world average is over 70 years. In some developing countries, particularly those worst affected by HIV/AIDS, such as Botswana, Niger, Malawi, and Zambia, life expectancy at birth has fallen to less than 40 years.
- 39 HIV/AIDS, TB and malaria also have a debilitating effect on the 250 million people who suffer from the diseases in developing countries, where prevalence rates are highest. Disaggregated data reveal that more than a third of adults in Botswana, and a quarter of adults in Lesotho, Swaziland and Zimbabwe, are infected. Table 2.1 shows the global distribution of adults living with HIV/AIDS.

Chart 2.1: Deaths from HIV/AIDS, TB, and malaria (1999)

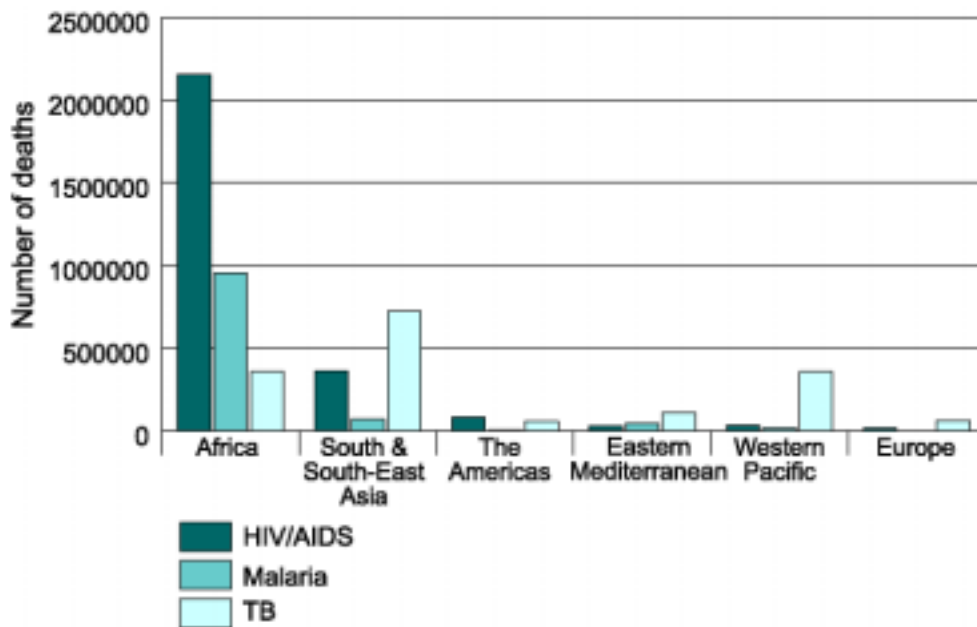


Table 2.1: Proportion of adults (15-49 years) living with HIV/AIDS (1999)

Region	Estimated numbers of adults infected with HIV/AIDS	% of adult population
Sub-Saharan Africa	23 million	8.6
Caribbean	0.4 million	2.1
North America	0.9 million	0.6
South & South East Asia	5 million	0.5
Latin America	1 million	0.5
Western Europe	0.5 million	0.2
Eastern Europe & Central Asia	0.4 million	0.2
East Asia & Pacific	0.5 million	0.1
North Africa & Middle East	0.2 million	0.1
Australia & New Zealand	0.02 million	0.1

2.3 ... and counter the social and economic consequences

40 At current levels of infection and death, the social and economic consequences of HIV/AIDS, TB, and malaria for the poorest countries - particularly those in sub-Saharan Africa - are devastating:

- seven million children in the developing world lost their mother or both parents to HIV/AIDS in 2000. 6.5 million of these children live in sub-Saharan Africa. The number of children orphaned each year is expected to rise to 17 million by 2010.
- TB killed 1.7 million people in 1999. TB sufferers are unable to work for an average 3-4 months and lose around 20 per cent of annual household income as a result. The macroeconomic implications are substantial, as 75 per cent of TB cases in developing countries occur among the economically active population, and estimates suggest that the cost of TB-related productivity losses is significant.
- malaria killed 1.2 million people in 1999, of whom most were young children and 90 per cent were African. Like TB, malaria has a substantial impact on the economically active population, resulting from and exacerbating poverty. One study comparing countries with high and low malaria prevalence suggests that effective malaria control could translate into an additional 3 per cent annual economic growth.

Future trends

41 Projecting future trends in HIV/AIDS, TB, and malaria in the developing world is difficult. Personal behaviour, particularly that which prevents the spread of infection, resistance of the disease organisms to existing medicines, and the possibility of more effective medicines in the future, mean that any projections are based on a range of assumptions.

- 42 In the absence of reliable data, it is widely accepted that if unchecked, the number of new cases and the consequences of the diseases will rise dramatically over the next decade and beyond.

Chapter 3: Existing action

Summary

- There is no shortage of initiatives to tackle these diseases – but efforts are poorly co-ordinated and action is fragmented.
- Substantially increased resources are needed to tackle the scale of the problem and to even come close to meeting agreed international targets for disease reduction.
- The international community has worked together successfully to tackle other communicable diseases –it must do so again.

3.1 There are many initiatives aimed at tackling the major communicable diseases ...

- 43 Besides the international donor agencies, there is substantial existing additional action to tackle HIV/AIDS, TB, and malaria. Box 3.1 shows the major existing global partnerships to improve health care systems and sponsor or manage research into new, more effective health products.
- 44 However, few of these initiatives provide and distribute existing health products on a significant scale, although the Global Alliance for Vaccines and Immunisation (GAVI) has committed \$90 million to 25 countries to purchase vaccines for a number of diseases, including Hepatitis B and yellow fever. GAVI has also supported a generation of new products and driven down prices for some drugs. However, there are no initiatives that establish incentives for the development of more effective health products by committing in advance to buy successful, highly effective new products as they become available.

Box 3.1 Examples of existing major global public-private partnerships

UNAIDS

The global mission of UNAIDS is to lead, strengthen and support an expanded response to prevent the spread of HIV, to provide care and support for those infected and affected by the disease, reduce the vulnerability of individuals and communities to HIV/AIDS, and alleviate the socio-economic and human impact of the epidemic. In 1996, six organisations joined in this co-sponsored programme - UNICEF, UNDP, UNFPA, UNESCO, WHO and the World Bank - and were joined in April 1999 by UNDCP. UNAIDS has an annual budget of \$60 million. UNAIDS is guided by a Programme Co-ordinating Board with representatives of 22 governments from all parts of the world, representatives of the 7 UNAIDS co-sponsors, and 5 representatives of non-governmental organisations (NGOs), including associations of people living with HIV/AIDS.

Box 3.1 (cont)**The International AIDS Vaccine Initiative (IAVI)**

IAVI's aim is to ensure the development of safe, effective and accessible HIV vaccines for use throughout the world, but particularly concentrating on those that could be used in developing countries. The organisation was established in 1996, with major participants being: developing countries, vaccine and biotechnology companies, academics and research institutions international agencies, non-governmental organisations, governments and private corporations. The organisation's major funders include the Bill and Melinda Gates Foundation, Rockefeller, Sloan and Starr Foundations, World Bank, UNAIDS, UK, Netherlands, Ireland, Canada and US governments, and other donors. The initiative works under the governance of an international board serving in their own capacity with members from 9 countries and with expertise from relevant bodies.

Roll Back Malaria Partnership (RBM)

RBM is the WHO's overarching strategy that focuses on co-ordinating the fight against malaria. Its aim is to provide global leadership, strategy and overall co-ordinating mechanisms to reduce the global malaria burden by 50% by 2010 through interventions adapted to local needs and strengthening of the health sector. It was established in 1998 and is hosted by a WHO secretariat.

Malaria Vaccine Initiative (MVI)

MVI's aim is to identify gaps and apply resources to ensure that a malaria vaccine is developed. Its mission is to accelerate the clinical development of promising malaria vaccine candidates and ensure that eventual vaccines are available and accessible to the developing world. It was established in 1999 and is an initiative of the Programme for Appropriate Technology and Health (PATH) whose Washington office administers the MVI secretariat. Partners are from the malaria research community including government agencies, academia, public and private research institutions and vaccine producers. It is funded primarily by a \$50 million grant from the William H Gates Foundation, and is guided by the Strategic Advisory Council and PATH's Board.

Multilateral Initiative on Malaria in Africa (MIM)

MIM's aim is to strengthen and sustain, through collaborative research and training, the capability of malaria endemic countries in Africa to carry out the research required to develop and improve tools for malaria control. MIM also aims to raise international awareness of malaria, to promote global communication and co-operation, and to ensure that research findings are applied to malaria treatment and control. It was established in 1997, and co-ordinated by a secretariat that rotates every few years among partner organisations.

Medicines for Malaria Venture (MMV)

MMV's aim is to foster and finance through public-public partnerships and discovery and development of one new technically appropriate, cost-effective, accessible and affordable antimalarial drug every five years. It was established in 1999 with major funders primarily from public and non-profit sources. Industry's contribution consists mostly of expertise and resources. The organisation works under the governance of a board made up from the public, non-profit and private sectors.

European Malaria Vaccine Initiative (EMVI)

EMVI's aim is to provide a mechanism through which the development of experimental malaria vaccines can be accelerated within Europe and in developing countries. It was established in 1998 by the European Commission with its secretariat at the Serum Institute in Copenhagen.

Box 3.1 (cont)

Stop TB

Stop TB's aim is to ensure that every person with tuberculosis has all the necessary information and access to treatment and cure. To protect vulnerable populations from TB and multi-drug resistant TB, and to prevent unnecessary social and economic tolls of the disease. It was established in 1998, and has over 100 global partners and funders. The organisation works under the governance of a co-ordinating board of 25 partner representatives, and the Global Stop TB Partners' Forum that meets every two years.

Action TB

Action TB is a 10-year programme funded by Glaxo Wellcome. Its aim is to identify new drug targets and vaccine candidates for TB, and surrogate markers for use in clinical trials. It was established in 1993 as an industry-academia partnership, along with public bodies including the US National Institutes of Health and the Howard Hughes Medical Institute.

Global Alliance for TB Drug Development

The aim of the Global Alliance is to accelerate the discovery and development of new TB drugs that will improve treatment regimes and be effective against multi-drug resistant strains of TB. It was established in 2000 as a not-for-profit organisation. Major participants and the board of directors come from all sectors, with major funders expected to be two-thirds from the private sector and one-third from public sources.

Gates' Children's Vaccine Program at PATH

Focusing on children's vaccinations and the Programme for Appropriate Technology and Health (PATH). This programme aims to ensure that all children receive the full benefits of new lifesaving vaccines within undue delay. Gates' CVP works to put immunisation at the top of the global health agenda, develops new financing solutions for immunisation, collaborates on research to provide reliable information for decision-makers, and supports new technologies to improve immunisation delivery. Oversight is provided by the PATH board, Strategic Advisory Council and Expert Review Group composed of international experts.

Global Alliance for Vaccines and Immunisations (GAVI) and the Global Fund for Children's Vaccines (GFCV)

These focus on the purchase of new vaccines for poorer countries. GAVI aims to consider applications to fund new vaccines from countries with populations less than 150 million and per capita GNP less than US\$1000. It was established in 1999 with a donation from the Bill and Melinda Gates Foundation of \$750 million. Further funding comes from the US UNICEF committee. The organisations are guided by the Working Group of the Global Alliance for Vaccines and Immunisations, a group involving national governments, WHO, UNICEF, World Bank, Rockefeller Foundation and IFPMA. The GFCV is the financing arm of GAVI.

3.2 ... but lack of co-ordination is a problem ...

- 45 As can be seen from Box 3.1, there are many initiatives in existence, but the action is fragmented and lacks the coherence needed to ensure faster progress. The increasing global interest in these diseases may lead to a proliferation of new initiatives, and without an over-arching management body, there is a danger of duplication, poor targeting, and a waste of resources. The WHO's Massive Effort Against Diseases of Poverty, launched in 2000, aims to unite partners to create action to facilitate sustainable development, stimulate

economic growth, ensure greater global public health security and, most importantly, save human lives.

3.3 ... as is a lack of resources ...

- 46 The WHO Commission on Macroeconomics and Health, established in 1999 and due to report in late 2001, has made estimates of the scale of global resources currently committed through initiatives such as those in Box 3.1. The Commission believes that the current level of resources falls far short of what would be needed to come close to meeting the Okinawa targets for reducing HIV/AIDS, TB and malaria by 2010.
- 47 Table 3.1 shows interim estimates of the annual shortfall in resources needed to tackle HIV/AIDS, TB and malaria. Broadly, additional annual funding of between \$9 billion and \$15 billion is needed to scale up the implementation of existing priority programmes to meet the Okinawa targets.⁺ An additional \$1 billion a year is likely to be required to stimulate research and development of new, more effective health products. Modelling analysis conducted by the PIU and Brookings for this report (see Annex 6) suggests that a figure towards the lower end of this range would be sufficient.
- 48 Only 10 per cent of global spending on health research is devoted to diseases that account for 90 per cent of the global disease burden. This means that current progress towards significant improvements in the effective use of available drugs, vaccines and other products to tackle the disease burden is too slow, and few breakthroughs for new products appear likely in the short-term. In addition, there are long periods of time required to make new products available.

Table 3.1: Estimates of the annual shortfall in resources available to tackle these diseases*

	Estimated current resources from external sources US\$ billions	Additional resources needed annually to scale up existing activity by 2007, within existing health systems US\$ billions
HIV/AIDS	3.0	5.0 to 7.3
TB	0.1	0.2 to 0.3
Malaria	0.3	3.5 to 7.4
Total	3.4	8.7 to 15.0

+ Investment needed by 2007, on the basis of current analysis being prepared for the Commission for Macroeconomics and Health.

* Notes for table:

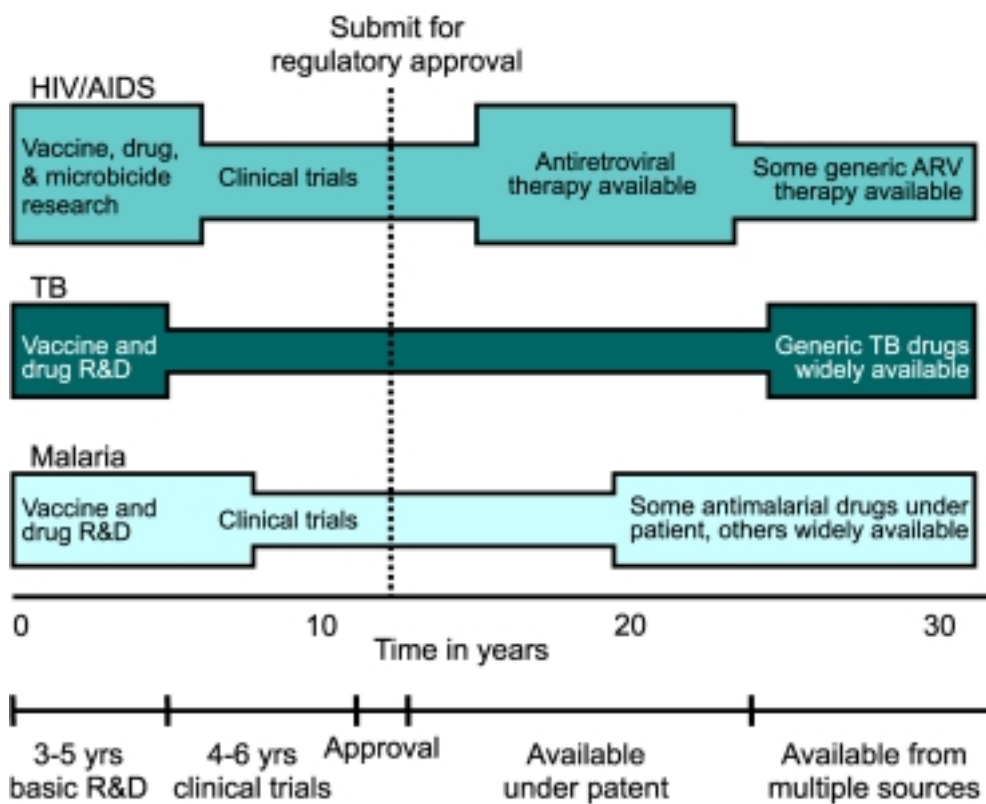
- Prices are not adjusted for inflation
- Estimates do not take into account a decline in the use of existing technologies if and when new, more effective technologies arrive.
- Figures should be treated with caution as the estimates may be understated where we have tried to avoid double-counting.
- Years of current estimates as follows HIV/AIDS 2001; TB 1999; Malaria 1998.

49 The representation of product development timelines in Figure 3.2 (overleaf) shows when new and effective products are likely to come to market, based on available information about current research, investment and progress.

3.4 A new global commitment is needed ...

50 Global disease control benefits the entire world's population, including those countries that have taken limited action to control the spread of disease within their own population. Since no one country has an incentive to tackle the full extent of the problem, there is an under-provision of the actions required to sustain a disease free environment. A co-ordinated strategy for future financial commitments to health is therefore necessary to control HIV/AIDS, TB and malaria.

Figure 3.2: Drug development time line



51 At the individual level, taking action to prevent disease, or breaking transmission through the use of vaccines, benefits not only the individual but also others, through the prevention of disease transmission and early clinical management. However, in making decisions about preventative measures, this aspect is unlikely to be valued - the individual will mainly consider only their own benefit and not that of the population in general. So, in the absence of public intervention, it is unlikely that preventative measures will be taken to the necessary degree.

52 Therefore, a co-ordinated strategy of increased promotion and awareness of preventative measures and available treatment, as well as the subsidising of products, is required.

development targets by noting that '*infectious and parasitic diseases, most notably HIV/AIDS, TB and malaria, as well as childhood diseases and common infections, threaten to reverse decades of development and to rob an entire generation of hope for a better future*'.

- 54 The international community has successfully co-ordinated its efforts before to tackle global communicable diseases. Substantial resources were committed over many years to fight polio and guinea worm, both of which are now approaching eradication. Onchocerciasis has also begun to be controlled. It is in everyone's interests that the international community should again act together to control the spread of HIV/AIDS, TB and malaria.

Chapter 4: The need for an holistic approach

Summary

- Health care systems in developing countries are inadequate and under-resourced. Efforts to tackle HIV/AIDS, TB and malaria should be integrated into national health systems and not established as vertical, disease-specific programmes. Developing country governments - with support from the development agencies - should prioritise health sector development.
- Those who need them most cannot afford health products to prevent or treat HIV/AIDS, TB and malaria. Many existing health products are also ineffective in the face of drug resistant disease strains.
- A package of policy measures is needed to strengthen measures for prevention and treatment and to improve and expand coverage of health care systems, and to ensure that new and existing health products to tackle HIV/AIDS, TB and malaria are affordable, and to incentivise the development of new, more effective products.
- By comparing the scale of the problem with the current response, it is clear that the international community will struggle to meet the Okinawa/Millennium targets. What is needed is an holistic approach that co-ordinates action and outcomes to tackle all aspects of the diseases of poverty.

4.1 Prevention and awareness have a major role to play ...

- 55 Public interventions to improve health can be very cost-effective. Interventions that reduce the incidence of communicable disease can produce large savings in treatment costs. For some diseases, public expenditure pays for itself even when the indirect benefits - such as higher labour productivity and reduced pain and suffering - are ignored. HIV/AIDS, TB and malaria all affect adults in their most productive years, and the infections resulting from HIV/AIDS - which include TB - increase demand for expensive health care.
- 56 Approved vaccines to protect against HIV/AIDS and malaria do not yet exist. The current vaccine against TB (Bacille Calmette-Guerin, or BCG) is almost 80 years old and, although protective for children, does not effectively protect adults against TB. HIV/AIDS prevention focuses largely on promotion of safe sex, use of condoms, together with fewer sexual contacts. All of these measures face behavioural, cultural and religious barriers. Preventing HIV infection is also important for TB, as a weak immune system causes the emergence of latent TB infection, which then poses a risk to others.
- 57 Current forms of prevention against malaria include personal protection measures, (eg. protective clothing, repellents, and treated bednets), or community protection measures (eg. the use of insecticides or environmental management to control transmission). This selective use of vector control is now understood to be the most cost-effective and sustainable form of

prevention. However, vector control can never be 100 per cent effective, so the appropriate use of safe and effective drugs is still needed.

- 58 There are a number of information failures associated with disease prevention and treatment. The relationship between patient and health care provider is complicated and is subject to variable rationales. A simplified example of this might be that a person knows when they are unwell and may be able to describe the symptoms of their illness, but they are probably unable to fully understand what is wrong with them without seeking medical expertise. However, a conflict of interest may arise between the patient's benefit and that of the health care provider who may have a strong incentive to prescribe the most profitable treatment. If the health care provider is linked to a product manufacturer this conflict may worsen, as there may be strong financial reasons for prescribing products even though they may not always be the most appropriate treatments. There is therefore a role for public regulation and publicly funded promotion and awareness raising campaigns so that people are able to make informed decisions about their health care.
- 59 There is evidence that communicable disease prevention and control works best when backed by strong government commitment. In Uganda, strong political commitment to tackling HIV/AIDS, including public support for promotion and awareness programmes, contributed to an 11 percent fall in HIV prevalence among pregnant women aged 13-19 years in just four years. In Senegal, the response to HIV/AIDS was swift, well-planned and far reaching. Political leaders took the initiative early on, openly discussing the issues. Safe sex education was integrated into the school curriculum and support obtained from the religious community. Condom use was promoted universally and treatment for sexually transmitted diseases (STDs) made widely available. As a result, young people in Senegal are not having less sex, but they are practising safer sex. HIV prevalence has remained low.
- 60 Evidence from Thailand suggests that prevention can also work once the HIV/AIDS epidemic has entered rapid growth. Alarmed at the rapid spread of HIV, Thai authorities discovered that a high proportion of men were having unprotected sex with sex workers. The government formed a partnership with brothel owners and sex workers to ensure 100 per cent condom use. Mass media campaigns discouraged commercial sex, and young women were offered better educational and vocational opportunities to keep them out of the sex industry. The holistic approach was a success; risky behaviour and the spread of HIV have declined, although prevalence is still unacceptably high.

4.2 ... improved health systems ...

- 61 Health systems in developing countries are often inadequate to ensure that advice and treatment is available to those who need it. 95 per cent of HIV/AIDS sufferers have no access to even basic health care. Only 20 per cent of TB sufferers receive effective treatment. Health systems need to be appropriately organised, managed and financed to deliver pro-poor health outcomes. They need to be staffed with skilled and motivated individuals who are prepared to work with poor communities, often in remote areas. Resource constraints make the efficiency and effectiveness of such health systems critical. Since 1997, the UK Department for International Development has

committed £1 billion to building primary health care systems. Governments should support the strengthening of health systems in both the public and private sectors.

- 62 All improvements to health care systems should be sustainable. An important lesson from previous disease-specific initiatives, including childhood immunisation, is that they cannot be sustained if they are not integrated into national health systems. It is essential to resist the temptation to establish vertical, disease-specific health care delivery initiatives to tackle HIV/AIDS, TB and malaria. Vertical initiatives appear attractive because they offer a faster route to tackling specific diseases by by-passing slow existing systems and bureaucracy. But vertical initiatives not only tend to operate outside existing delivery systems, but by diverting human and financial resources, they actually undermine existing health care delivery. They are also susceptible to the changing priorities of external public and/or private sector support.
- 63 There is an emerging international consensus on how best to build more effective and sustainable health systems and services in developing countries. Key elements include:
- country-led health strategies as part of broader poverty reduction strategies;
 - upgrading and expanding existing health systems using public and private sector health care providers;
 - addressing the causes and not just the symptoms of ill-health;
 - removing barriers which prevent the poor accessing health services; and
 - ensuring standards, accountability and responsiveness to users' needs.
- 64 Existing resources are insufficient to support the expansion of effective health care systems. In Sub-Saharan African, annual total expenditure on health ranges from \$268 per capita in South Africa to as little as \$5 per capita in Mozambique and Niger. Average annual expenditure per capita is \$36 per capita) Governments in developing countries need to ensure that public expenditure is appropriately prioritised between sectors in poverty reduction strategies, and, within the health sector, between expensive, high-technology hospitals in urban areas and universal primary health care. Involving the private sector in health sector strategies is one way to begin to meet unmet health needs. In developing countries, the private sector plays a major role in health care provision, but the World Health Report 2000 states that many governments are unaware of the extent of private provision of health care services, and they need to step-up the regulation of the private sector. The developed world must provide support, resources, practical help and training where it is needed.

4.3 ... and affordable and effective health products

- 65 To tackle HIV/AIDS, TB and malaria, health systems need both more affordable and more effective health products to deliver, and also to use more effectively those that exist already. Health products include vaccines, diagnostics, and treatment drugs, as well as non-pharmaceutical products such as condoms to prevent the spread of HIV, and treated bednets to prevent

transmission of malaria by mosquitoes. As set out in Chapters 1 and 2, communicable diseases - and HIV/AIDS, TB and malaria, in particular - disproportionately affect the poor in developing countries. Countries where annual per capita expenditure on health is as low as \$10 cannot afford to purchase vaccines and treatment drugs from the health budget, even if pharmaceutical companies drop their price per dose (excluding delivery costs) close to zero.

- 66 Given the extreme poverty of those living on less than \$1 a day, only a very small proportion of household income can be dedicated to health. Neither the public sector nor households in developing countries can afford to purchase an adequate supply of existing health products to prevent or treat communicable diseases. Those most at risk from HIV/AIDS, TB, and malaria are those least able to pay for the available preventative and treatment products.
- 67 The efficacy of many treatment drugs for TB and malaria is decreasing, as the diseases become increasingly resistant to them. There are signs that increasing numbers of people are infected with multi-drug resistant strains of TB (MDR-TB). MDR-TB occurs where the strain of TB is resistant to the two most important treatment drugs, isoniazid and rifampicin. In industrialised countries, TB treatment costs around \$2,000 per patient, but rises to as much as \$250,000 per patient for MDR-TB. People infected with TB do not become ill immediately, as the immune system protects against the disease. Only when the immune system is weakened, for example by infection with HIV, does illness occur. The full course of treatment for TB lasts up to six months. MDR-TB is caused by incomplete treatment. Patients do not complete the prescribed course either because they start to feel better, or because the intensive regime and inadequate supervision in poor health care environments makes it difficult. Existing drugs for the treatment of HIV can be effective in some conditions, but this is dependent on a rigorous treatment regimen and a reliable health system.
- 68 The cost-effectiveness of existing and possible future health products varies enormously. The estimated cost of each additional DALY saved for existing and possible future products is shown in Table 4.1 (overleaf). The data indicate that vaccines would be the most cost-effective health product by an order of magnitude. Existing preventative products, such as condoms and bednets are significantly cheaper than existing treatments for HIV/AIDS and malaria, although still beyond the reach of many. New generation treatment drugs should be cheaper, better and more feasible options than existing treatment drugs, particularly for HIV/AIDS.

New health products

- 69 The obstacles to deploying many treatments are large, and failure to complete treatment promotes drug-resistant strains of disease. Many argue that the best hope lies with the prospect of more effective vaccines and drugs in the future. New vaccines in particular could potentially lead to dramatic, sustained reductions in disease prevalence. However, new research into drugs and vaccines to tackle these diseases is limited. Our best estimates suggest that a new vaccine for these diseases that is suitable for use in developing countries is still some way off (see figure 3.2)

70 The main reason for this lack of research is that HIV/AIDS, TB and malaria are diseases that disproportionately affect the poor. While HIV/AIDS is also a health problem in rich countries, the clade of HIV that is most common in Africa (clade C) differs from the clades most prevalent in developed countries. It is unclear – and commonly presumed unlikely – that a vaccine developed to fight the clades common in developed countries would also be effective against clade C. In poor countries, neither households nor public sector health budgets can afford to purchase sufficient health products to prevent and treat diseases. Thus, although there is considerable *need* for health products to address these diseases, this does not manifest itself in an actual *market* (effective demand*) for these products. Without customers who are able to pay for the products, there is very limited incentive for the pharmaceutical industry to engage in research and development for new products to tackle these diseases that are appropriate for developing countries. Given the large social and economic benefits to society from reducing the burden of these diseases, public intervention to create an effective market is warranted.

Table 4.1: Cost-effectiveness of existing and future health products⁺

Existing health products	Expected cost per additional DALY saved (US\$)	Possible future health products	Expected cost per additional DALY saved (US\$)
Nevirapine	14	HIV vaccine	1
AZT	619	TB vaccine	4
Anti-retrovirals	1321	Malaria vaccine	3
Condoms	25	HIV drug	20
Multiple doses of TB drug	76	TB drug	23
Single dose of malaria drug	34	Malaria drug	22
Bednets	14	–	–

Note: Caution needs to be exercised in making cost-effectiveness comparisons across these products which are based on a combination of current market prices, and estimates of effectiveness and future prices. These estimates are useful for making very broad comparisons, and should be interpreted as orders of magnitude only.

71 However, creating an effective market is not in itself enough. Research into new drugs and vaccines is a public good in the sense that knowledge

* Effective demand represents not only the need for a technology but also the ability to pay for it. Hence in the countries most affected by these diseases there may be considerable need for these products but not the income levels required to translate this need into effective demand.

⁺ Notes for table

- Estimated DALYs saved from existing health products derived from the literature review performed by the derived from Brookings Institution and PIU
- Nevirapine and AZT can only be used by pregnant mothers, so the maximum spent in any one year on these products is estimated to be \$3.6m and \$3.1m.
- Expected cost of new technologies based on \$1 billion expected cost using an advance purchase fund. These cost estimates are contingent upon the method of funding and are predicted to be higher is a different instrument is used to provide incentives for R&D.
- Estimates based on average cost of multitude of drugs used.

generated by research is virtually costless to disseminate⁺ and limitless in the number of beneficiaries. Since the first company to invest in R&D will quickly see the benefits of this knowledge shared by its competitors, there is little incentive for it to carry out this research, even though society would benefit from the knowledge it produces. This under-provision of research suggests two possible forms of government intervention. The first is that direct public funding of research may be warranted. The second is that the government should set in place provisions that temporarily exclude others from the benefits of research, for example through the use of patents (see Chapter 7).

- 72 Research is also subject to “time consistency” problems. Research into new pharmaceuticals is very expensive, but once products have been developed they can usually be manufactured at relatively low costs. Armed with this knowledge, governments may be tempted to use their buying power to try and obtain these products at a price that covers the manufacturing costs but not the research costs or the costs of bearing the risk that research efforts might fail. If a pharmaceutical company suspects that governments might use this strategy, this lowers the incentives for a firm to invest in new technologies. This suggests that governments should take steps to ensure credibility in the purchase of new technologies at a price that covers not only the cost of manufacture but also the costs and risks associated with research. An advance purchase commitment would be one way of signalling this commitment.

The way forward

- 73 A global strategy is needed to take forward this holistic approach. The strategy will need to improve health systems and to ensure that new and existing health products to tackle HIV/AIDS, TB and malaria are affordable, and to incentivise the development of new, more effective products. The key elements of such a strategy are outlined in Chapter 5.

⁺ If disseminated via the internet the cost of sharing information is practically zero. It is therefore very difficult to prevent the rapid dissemination of the results from R&D.

Chapter 5: Key elements of a global strategy

Summary

- In order to meet the Okinawa/Millennium targets, an holistic approach is needed, including a range of measures to improve health care systems and health promotion; to address barriers to affordability of existing health products; and to strengthen incentives for the production of affordable and effective new products.
- The key elements of a global strategy for taking this forward include additional support to improve health care systems and health promotion; a Global Fund for Health to finance the purchase of health products required to tackle HIV/AIDS, TB and malaria; clarification of the role of intellectual property protection, wider and more effective use of voluntary licensing, and increased support for basic and applied research.
- Such a strategy needs to be backed up with the necessary political and financial commitment, and action from a wide range of partners inside and outside government. It needs to complement action by developing countries to develop and strengthen their own health strategies.

74 Building on the holistic approach outlined in the previous chapter, this chapter considers the key elements of a global strategy to tackle the disease burden, involving action to:

- improve health care systems and health promotion, in particular:
- to ensure universal access to diagnosis, treatment and care; and
- to raise awareness of disease risks and how to avoid them, to reduce transmission and numbers of new cases.
- make existing health products more affordable to those who need them; and
- encourage additional research into new, more effective and affordable health products including drugs and vaccines.

5.1 Additional support is needed for health care systems and health promotion ...

75 The importance of promotion and awareness campaigns backed by strong political leadership, and support to improve and expand health care delivery systems, was outlined in Chapter 3. Developing country governments need to take the lead in determining how best systems can be upgraded and coverage expanded. The developed world must provide support, resources, practical help and training where it is needed and according to national health strategies.

76 Support for health care systems and health promotion is a key element of country-led poverty reduction strategies, and bilateral and multilateral

assistance. Setting out the UK Government's strategy for achieving the health-related international development targets, the Department for International Development points to emerging international consensus on how this can most effectively be achieved so as to:

- address underlying causes of ill-health;
- ensure access to health services for the poor;
- assure standards, accountability and responsiveness to existing and potential health service users;
- strengthen the state in its role as regulator and provider of services for the poor; and
- encourage the private-sector delivery of appropriate health services to the poor.⁺

77 However, as argued earlier, current resources are insufficient. Annual expenditure is as low as \$10 per capita in some countries and in 2000 only 5% of total official development assistance was spent in the health sector*.

78 **Recommendation: together with developing country governments, private sector and non-governmental partners, additional efforts are needed by developed country governments and multilateral institutions to scale up assistance to the health sector.** Health strategies need to be country-led and backed with increased government and development assistance resources dedicated to the health sector. These additional resources should be prioritised to health promotion, cost-effective prevention policies, and scaling up delivery systems (including infrastructure and trained staff), to ensure universal access to a minimum standard of primary health care.

79 Considerable analysis of how best to secure stronger, more responsive and more effective health care delivery and promotion has been undertaken by the World Bank, the UK Department for International Development and others in the international community.[¶] The UK view of how best additional resources can be channelled through bilateral and multilateral co-operation is set out in the DFID strategy paper '*Better health for poor people*'.

5.2 ... as are measures to improve affordability and incentives for new products

80 The remainder of this report therefore focuses on the issues of how best to improve affordability of health products, and incentives to produce affordable and more effective products.

⁺ Department for International Development, UK: *Better health for poor people* (November 2000).

* OECD official development assistance figures for 2000

[¶] For example, the World Bank's influential report *Assessing Aid: what works, what doesn't and why* (1998) sets out generic lessons concerning the importance of a sound policy environment and effective public institutions, which are of particular relevance in the health development context.

5.3 Gaps in current action and blockages to progress need to be addressed ...

81 Our analysis in Chapter 4 points to a number of gaps in current effort to make progress towards more effective products; and to improve affordability. A global strategy needs to contain a package of measures which correct for these gaps. The gaps identified are summarised in Box 5.1.

Box 5.1: Gaps and blockages in current action to tackle affordability and incentives

- A lack of effective demand for products caused by the poverty of those in most need;
- Weak incentives for extra investment in basic research, reflecting the public good aspects of such research;
- Weak incentives for investment in research and development result in slow progress towards the development of new vaccines, drugs and other products for these diseases;
- Blockages in progress at the clinical trials stage;
- Delays in progress to market caused by variations in national product regulation, and by regulatory capacity; and
- A lack of co-ordination between existing fragmented initiatives needs to be addressed to improve the rate of progress and ensure better use of resources.

5.4 ... a large number of possible policy measures exist ...

82 We have assessed a wide range of potential policy measures which could contribute to a package to address these, which could be adopted by the international community. Box 5.2 summarises the full set of policy options considered. Each measure has been assessed against a set of criteria to establish its likely contribution to delivering the targets.

Box 5.2: Full list of possible instruments considered

(see box 5.4 for the package identified as most promising)

- **Global advance purchase fund** (including milestone payments and co-payments). An international commitment to purchase new technologies.
- **Global advance purchase fund** with auction of tradable participation rights.
- **UK Tax (pull)**. Firms receive a tax credit to match qualifying sales of product.
- **Global current purchase fund/direct subsidy**. Making existing technologies available at below market price through purchasing/directly subsidising.
- **UK/international public funded research**. Direct funding of research (includes discovery and development) and public private partnership arrangements.
- **UK/international clinical trials support**. Use of public funds to reduce cost/risk of clinical trials.

Box 5.2 (cont)

- **UK tax (push).** Allows a set % of R&D expenditure to be offset by increase threshold non-taxable income.
- **International tiered pricing.** Encouraging/facilitating market segmentation to enable cheaper prices for developing countries for existing products (includes market segmentation within developing countries)
- **International harmonisation regulations.** Harmonising procedures for licensing products (enabling products reach market earlier) and procurement rules (enabling better supply).
- **Developing countries import duties.** Removal or reduction of import duties on phase I to III compounds, bednets, etc.
- **Developing countries production through voluntary licensing.** Local production of patented drugs through voluntary licensing under TRIPS.
- **Compulsory licensing.** Local production of patented drugs through compulsory licensing.
- **International award for development.** World-wide recognition of pharmaceutical company and individual efforts.
- **Developed world support.** Campaigns/public awareness raising to secure support for action from developed world.
- **International fundraising.** Funds for R&D or purchase raised by global lottery or surcharge on related products.
- **International IPR extension.** Allowing longer intellectual property exclusivity for relevant new products.
- **International roaming exclusivity.** Similar to above except patent extension granted on an unrelated (revenue earning) product.
- **Developing country production (generics).** Using international development assistance to directly finance or subsidise generic industry in developing countries
- **Links to debt relief.** Funds saved from debt relief used to purchase vaccines, drug, etc.
- **International cash prize.** A competition announces a cash prize on a specific date, which is then awarded to the company who comes closest to the desired outcome.
- Measures to improve the quality of developing countries' generics.
- International competition in generics industry.
- International or domestic **support for small companies.**
- International pharmaceutical donations.

5.5 ... policy options need to be assessed against a set of key criteria ...

- 83 These criteria are summarised in Box 5.3. They attempt to establish the extent to which each measure will impact on affordability; additional research and development and the speed at which new health products are likely to come to

the market; and ultimately, whether they are likely to maximise reductions in the disease burden, for the money spent.

- 84 Our assessment has included a quantitative analysis of the likely improvements in health outcomes, using a measure of death rates and impacts of disease on quality of life (DALYS), under a range of possible levels of intervention or resource commitments. These findings are based on assumptions reflecting the uncertainty surrounding estimates of future disease trends, and the expected effectiveness of different health products to prevent and treat HIV/AIDS, TB, and malaria. This enables us to indicate some of the key choices to be made, both about the mix of policy measures required, and the level of resources needed to secure health improvements.

Box 5.3: Criteria for selection of policy measures

Key questions in evaluating each policy measure:

1. Is it effective?
2. How much will it cost?
3. Is it the most cost-effective measure to deliver health outcomes?

Decision criteria:

4. Will it result in new health products for developing countries?
5. Will new health products be affordable to developing countries?
6. When will an affordable new health product arrive?
7. What are the side effects?
8. Does it lend itself to an international solution?
9. What will be the burden sharing (leverage)?
10. Will the international community have to pay more than necessary for the outcome (deadweight loss)?
11. What will be the benefit?
12. What will be the cost?

Assumptions

- 85 Any assessment of options for addressing the health burden in developing countries must reflect the high degree of underlying uncertainty around many aspects of both the problem and the potential solutions. Projections of future changes in the underlying prevalence of disease are highly uncertain; as are take-up and pricing of existing products. There is particular uncertainty around the speed and outcomes of scientific progress towards new more effective health products. While stronger incentives for research and development can dramatically improve the prospects that major advances – such as a vaccine to immunise against HIV/AIDS - will emerge in the next decade, there is no certainty that they will do so.
- 86 These uncertainties have been reflected in the analysis by considering the effects of policy options under a wide range of plausible assumptions, before

reaching conclusions on which are the most likely.⁺ Key uncertainties reflected in a range of assumptions include:

- the existing state of science, for example the probability that it is impossible that a new drug or vaccine could be developed;
- the likely effectiveness of new products, including such factors as efficacy levels, the number of doses that must be administered and the time until disease become resistant to new products; and
- the coverage rates that new products are likely to achieve, including consultation and treatment rates for new drugs and coverage between different sectors of the population for vaccines.

Any uncertainty in the proposed design and institutional arrangements for policy measures is reflected by allowing a degree of flexibility to respond and to adapt as new information becomes available.

5.6 A global strategy – the package of measures

87 The analysis summarised in this report sought to bring together:

- the gaps or blockages in current activity to make existing health products more affordable for the poor and to encourage additional research and development effort to produce new, more effective health products (box 5.1);
- the range of policy measures which might contribute to addressing these gaps or blockages (box 5.2); and
- the criteria for assessing the policy measures (box 5.3).

Box 5.4 summarises the results of the analysis. It sets out the gaps and blockages that need to be addressed by the international community, and then the package of measures that offer the best means of doing so. These measures, taken together, offer the best prospect of achieving rapid, substantial and sustained reductions in the burden of the HIV/AIDS, TB and malaria. Some measures address more than one gap.

⁺ The modelling undertaken is described in Annex 6 to this paper.

Box 5.4: How the package of measures addresses gaps and blockages in current action to tackle affordability and incentives

Gap or blockage in current activity	Measures in the proposed strategy that correct for each gap or blockage
Lack of effective demand	<ul style="list-style-type: none"> • Global Fund for Health • Tax incentives for product donations • A framework for tiered pricing • More widespread and effective voluntary licensing
Weak incentives for investment in research and development	<ul style="list-style-type: none"> • Global Fund for Health (advance purchase commitment) • Clarity on the terms of intellectual property protection • Targeted public support for R&D • Tax incentives for R&D • Public-private partnerships for R&D
Weak incentives for extra investment in basic research	<ul style="list-style-type: none"> • Support for basic and applied research
Blockages in progress at the clinical trials stage	<ul style="list-style-type: none"> • Establishing a clinical trials platform
Regulatory delays	<ul style="list-style-type: none"> • Harmonising the regulation of new products
Fragmentation of initiatives	<ul style="list-style-type: none"> • Global Fund for Health

88 Recommendation: The international community needs to take action which:

- significantly scales up resources to purchase effective health products which those in most need cannot themselves afford;
- establishes strong incentives for extra investment in research and development to accelerate progress towards the development of new vaccines, drugs and other products for these diseases;
- strengthens support for basic research;
- addresses blockages at the clinical trials stage of pharmaceutical product development;
- reduces delays caused by variations in national product regulation; and
- improves co-ordination between existing initiatives.

89 There is already considerable debate about the precise form of action in these areas. As a contribution to ongoing international policy discussions this report makes a number of recommendations. Chapter 6 of this report addresses the issue of how to channel resources to improve affordability and strengthen incentives, considering a range of operational and institutional options for a Global Fund for Health (including an advance purchase commitment) in more

detail. Chapter 7 then looks at issues to be considered for other policy measures including intellectual property rights, tiered pricing, research and development and product regulation.

- 90 A new Global Fund for Health would finance the purchase and supply to the poorest of existing health products. It would also help to incentivise research and development of new products by establishing demand for the most effective products for tackling the diseases on the market at any particular time. These incentives could be substantially strengthened by an *advance purchase commitment* – a binding promise to purchase new, substantially more effective products, meeting pre-specified efficacy and cost-effectiveness criteria.
- 91 The Global Fund for Health – including an advance purchase commitment - requires a substantial and sustained political and financial commitment. As made clear above it also requires developing countries' health strategies and healthcare delivery systems to be sufficiently robust to ensure that newly-available products are deployed to those most in need and to maximise their impact on national disease burdens. Chapter 6 sets out a range of operational and institutional options for putting these measures in place.
- 92 Chapter 7 examines other measures that would, in our view, need to be put in place to secure the best prospect of rapid reductions in the disease burden. A strategy should include measures to complement the incentives provided by a Fund and advance purchase commitment – such as increased support for basic and applied research through a combination of tax incentives, establishment of a clinical trials platform and harmonisation of regulation. The strategy will also need to address how to facilitate the increased use of patented medicines at affordable prices while protecting intellectual property. This could be achieved via global agreement on the interpretation and use of TRIPS flexibilities, together with a framework for tiered pricing of patented products, and for greater use of effective voluntary licensing agreements allowing appropriate local production; all of which will help to improve affordability.
- 93 Greater coherence and co-ordination is needed across initiatives to address affordability and incentives. Action and resources are currently fragmented across a number of institutions, and while there are examples of strategic use of resources to achieve the fastest progress towards the development of new, affordable health products, there is weak overall co-ordination. The proposed Global Fund for Health will help to co-ordinate existing initiatives by virtue of its role in channelling substantial resources. However, **it is a priority for the international community to consider what more should be done to achieve greater coherence across existing initiatives.**
- 94 The measures set out in Chapter 7 are complementary to the Global Fund for Health. They should be regarded as part of a wider package of measures, targeted at different parts of the picture of gaps and blockages to progress, thus enhancing the overall effectiveness of action by the international community. They - like the Fund - require a new commitment to deliver through partnership of a wide range of players – including governments in the developed and developing world, multilateral and bilateral programmes, private sector producers, researchers, donors, and foundations; academics,

and the voluntary and social sectors. Chapter 8 sets out a “call to action”, identifying the key roles each of these parties will need to play, and the commitments they need to make, to secure a real and lasting improvement in health outcomes for the world’s poorest.

Chapter 6: Specific policy proposals – a Global Fund for Health

Summary

- A Global Fund for Health should be established to buy existing health products to tackle HIV/AIDS, TB and malaria in developing countries.
- The Global Fund for Health should include an advance purchase commitment to buy new, more effective products as they become available.
- The underpinning principles and specification of a Global Health Fund should be agreed by international consensus.

6.1 A Global Fund for Health is a key part of a strategy addressing affordability of existing products and incentives to develop new ones ...

95 ***Recommendation:*** a Global Fund for Health should be established, buying existing effective products to tackle the diseases, and including an advance purchase commitment to buy new, more effective products as they come onto the market. This will serve the dual purpose of:

- providing an effective mechanism for financing provision of health products to the poorest in developing countries, and
- ensuring that incentives are sufficient to secure the substantial increase in investment in research and development of new products needed to make substantial rapid inroads into the disease burden in the future.

6.2 ... both through buying existing products (“current purchase”) ...

96 The vast majority of the health products essential for developing countries to improve health and reduce the burden of disease, are produced off-patent (generic versions exist) at competitive prices. A direct financing arrangement is needed to improve the affordability of existing generic products beyond the level of competitive prices.

97 Once a patent expires, the patent holder no longer has the exclusive right to market the product, and competitors can enter the market. Basic economics tells us that in a competitive market, prices will be driven to the lowest level that allows for a reasonable return to be made to the firm. Although the pharmaceutical industry is not perfectly competitive (high start-up costs limit the total number of global firms) there are no regulatory barriers to entry and the pharmaceutical industry is becoming increasingly competitive with new firms from the biotech sector and middle income countries. For developing country products though, firms will be willing to supply only if there is a market for the product in the first place.

98 A Global Fund for Health could therefore play a significant role in making existing commodities available to those who need them in the poorest countries. In developing proposals for a Global Fund for Health the international community will need to consider a range of issues for specification. These should be developed through a process of consultation with all key stakeholders including developing countries. Much of the detail, such as what should be the Fund's immediate priorities and methods for dispersal, should be determined by the Executive Board of the Fund once it is established. Our preliminary views on the principles underlying a Global Fund for Health and how it could be specified are summarised in Boxes 6.1 and 6.2 below, and in greater detail in the attached Annex 2.

6.3 ... and through an “advance purchase commitment” to buy more effective products in the future ...

99 As well as purchasing existing products, the Global Fund for Health would also provide an incentive for *new* research and development by demonstrating a commitment to buying the most effective available products for tackling the diseases and establishing effective mechanisms for doing so. Experience with GAVI has shown that a substantial current purchase commitment can act as an incentive to industry to invest in the development and scaled-up production of new products. The more explicitly the rules governing the Fund specify that procurement will shift over time, to ensure new, more cost-effective products are purchased as they become available, the clearer the incentives to developers of new products.

100 With this clear commitment to purchase new products once available, the Global Fund for Health would provide a major incentive for research and development (R&D) by ensuring that there is a *future market* for the more effective health products needed. To be an effective incentive for R&D this commitment must be credible and must represent a commitment of resources beyond the annual budget for purchasing existing products.

101 Our quantitative analysis suggests that an advance purchase commitment is the most cost-effective means of encouraging the development of new health products. Crucially, funds committed to the advance purchase commitment would not be spent until more effective health products are developed. Scientists working on development of a product would receive nothing until an effective product is developed, thereby incentivising them to undertake research that will lead quickly to viable and marketable health products.

Box 6.1 Principles of a Global Fund for Health

The Fund should be underpinned by a number of principles agreed by the international community. Draft principles, based on those developed and agreed at the Okinawa International Conference on Infectious Diseases (December 2000) are:

- early inclusion of developing countries to ensure their full involvement in design and participation in the governance of the Fund. Products purchased through the Fund should be in response to developing countries' requests, be suitable for delivery in developing countries and be cost-effective;
- a light governance structure that encourages drive and leadership, keeps decision-making close to developing countries and enables them to play a major role in governing the Fund, be involved in resource allocation decisions, and monitor health improvements;
- to support and build on existing country-led health strategies and integrate with broader development processes, including poverty reduction strategies and sector-wide approaches. The planning burden and transaction costs to developing countries should be minimal;
- to be a truly global partnership – drawing in donations from governments, foundations and the private sector. It should not rely on or be dominated by any one donor. It should be transparent, driven by the need to deliver better health outcomes, and governed by principles supported by all;
- making products available and affordable to all those that need them. The Fund will not provide support for health systems. Instead, health systems should be strengthened through existing health sector programmes to enable products to be delivered;
- focusing first on the poorest countries with the highest burden of disease and setting out clear conditions for eligibility;
- sustainability through a long-term commitment to tackle diseases in developing countries.
- lesson-learning to facilitate rapid implementation and scaling-up responses to the diseases, through effective evaluation and peer review, so the effectiveness of strategies can be improved rapidly;
- promote co-ordination of product provision to developing countries.

Box 6.2 Key issues for Global Fund for Health specification

Resource requirements

A Global Fund for Health would need to be big enough to have a real impact and would need to increase incrementally as developing countries' capacity increases. Our analyses suggest that a substantial scaling-up in the order of billions of dollars is required.

Eligible diseases

Chapter 2 set out that communicable diseases are a major killer of poor people in developing countries. A Global Fund for Health should focus on communicable diseases, and in particular on HIV/AIDS, TB, malaria and childhood communicable diseases. In addition, making *effective health products* available for these diseases will make a significant difference to health outcomes.

Eligible expenditure

A Global Fund for Health should focus on adding value where there is a clear gap in existing action, i.e. making effective health products available to those that need them but cannot currently afford them. The new Global Health Fund should focus on purchasing **health products** that are cost-effective, appropriate for delivery in, and requested by, developing countries. Health products should include not only treatment drugs but also other products vital for prevention and diagnosis, including condoms, HIV testing kits and simple diagnostics.

Prices

A Fund would be in a strong position to negotiate reasonable prices for bulk purchase of health products, and should follow best-practice in procurement, ensuring as far as possible competitive, fair, open and transparent procedures.

Eligible countries

The Fund should be for those most in need. This will enable it to have the greatest impact. It should focus first on the poorest countries with the highest burden of disease. To be eligible countries should demonstrate political commitment to reducing communicable diseases - particularly HIV/AIDS, TB and malaria - in health sector strategies; and have a minimum health care delivery systems capable of ensuring products reach the poorest.

Contributors

The Fund should be a truly global partnership – drawing in donations from governments, not-for-profit organisations and foundations. Foundations are already very active in this area and the Fund should welcome their continued presence. The wider private sector could also be a source of potential donations to the Fund and ways of involving the private sector should be explored further.

Governance

The Fund should maximise use of existing national systems and processes, including the Poverty Reduction Strategy process. National policies and priorities should be supported. In setting in place the governance structures of the Fund, the international community should draw on and learn from the experiences of setting up other international initiatives, for example the Global Environmental Facility and the Global Alliance for Vaccines Initiative. The governance of the Fund will need to include a governing body representing key stakeholders, effective administration and country level mechanisms.

Box 6.2 (cont)

Possible options for the organisation of the Fund include:

- a small, high-level Executive Board of key stakeholders, including representatives of developing countries, funders and multilateral agencies;
- a small secretariat to support and report to the Executive Board;
- technical advisory inputs from key multilaterals and others; and
- banking and fiduciary functions housed in an institution such as the World Bank.

Accessing funds:

Developing countries need to be able to access funds in a way that minimises additional administrative burdens.

Dispersing resources:

Resources need to be dispersed to countries in the most efficient way, minimising transaction costs and opportunities for fraud. Increasing long-term funding to existing procurement mechanisms can drive down prices of essential commodities. An alternative would be for the Fund to purchase products directly from suppliers, in response to requests from developing countries for particular products. This would enable the Fund to use its purchasing power to negotiate reasonable prices.

- 102 ***Recommendation:* the establishment of an international advance purchase commitment as an integral part of the Global Fund for Health. In developing proposals for the advance commitment the international community will need to consider a range of issues for specification as summarised in box 6.3 (and set out in more detail in Annex 2). In particular, it is be important that national governments consider creatively how best to establish a credible long-term commitment within existing budgeting frameworks, while ensuring that effective financial control is maintained.**

Box 6.3 Advance purchase commitment specification

Commitment size:

The commitment must be large enough to act as a sufficient incentive for firms to undertake R&D. There is a lack of clear evidence of the size of market needed to incentivise R&D. Estimates range between an annual market size of \$100 million and \$500 million (real terms) per product. Above this minimum size, the larger the commitment the greater level of R&D that will occur and so the earlier new commodities are likely to be developed.

Products and diseases:

To be credible, the commitment must clearly state which diseases it will purchase new health products for and the specific health products that it will purchase. As discussed in Chapter 2, there is a clear rationale for focusing initially on HIV/AIDS, TB and malaria. To provide clear incentives it may be necessary to specify in advance the proportion of the commitment that will be dedicated to each disease. Our analysis suggests that a commitment to purchase new vaccines will have the greatest impact. However, drugs are also necessary for treating those already infected. Treatment of those infected can also reduce new infections.

It should specify in advance that products eligible for purchase must:

- meet safety specifications such as approval by regulatory bodies;
- be cost-effective with an expected impact on health outcomes significantly above existing products; and
- be requested by a developing country.

The commitment would be activated when an eligible product became available.

The price that will be paid for products:

Firms need to be sure that once they have produced a new product they will receive a price for it that will enable costs to be recovered. In addition, the commitment could specify a maximum cost per person immunised/treated. This would provide firms with an indication of the returns they will receive on their investment. The Fund might alternatively purchase the patent.

- 103 Our quantitative analysis demonstrates that an annual current fund of \$1 billion⁺ annually for 20 years, and an advance purchase commitment of \$10 billion to be paid as new products become available would save an expected 0.7-1.8 billion (1.5 billion central estimate) DALYs by 2010. Of that, 0.3-0.7 billion would be in HIV/AIDS, 0.2-0.4 billion in malaria, and 0.2-0.7 billion in TB. In other words, a total global fund of \$30 billion over 20 years, would reach between 44%-110% (90% central estimate) of the HIV/AIDS target, 55%-110% (90% central estimate) of the malaria target, and 35%-103% (85% central estimate) of the tuberculosis target – which is equivalent to between 25-60 million (53 million central estimate) lives.

⁺ to be paid in line with inflation

Chapter 7: Specific policy proposals – intellectual property, tiered pricing, research and development and regulation

Summary

A wider package of measures, targeted at different parts of the picture of gaps and blockages to progress should include:

- clarification of the flexibilities in intellectual property protection under the WTO TRIPS agreement, through global discussion on the terms under which they can be used; more widespread and more effective use of voluntary licensing agreements to allow local production; a framework for tiered pricing of patented products;
- tax credits for R&D; a clinical trials platform; harmonisation of regulations to speed-up product approval; targeted financial support and public-private research partnerships.

7.1 A range of measures is needed to tackle all of the gaps in current action ...

104 As discussed above, the Global Fund for Health forms a key part of a strategy to tackle prevalence of HIV/AIDS, TB and malaria. But it is not sufficient in itself to address all of the gaps in, and blockages to, effective action to tackle the affordability of existing products and provide sufficient incentives for the development of new, more effective products. This requires a number of other policy measures to be implemented alongside the Fund.

7.2 Clarity is needed on the terms of intellectual property protection

105 The first step in addressing access to essential medicines should be to establish a mechanism to assist developing countries in purchasing existing health products and making these more affordable. Consideration needs to be given to how to facilitate lower prices of patented products for developing countries, while maintaining the appropriate incentives for the industry to invest in research into new health products. One such policy recommended is a framework for tiered pricing which is explored in the next section.

106 The issue of affordability of patented products is inextricably linked with the role of intellectual property protection. The market failures noted in Chapter 4, which lead to sub-optimal investment in research, make the protection of intellectual property essential to ensure that sufficient incentives exist for firms to invest in research and development of new products offering significantly improved effectiveness in treatment and prevention. For most health products the protection takes the form of

patents, and the 'global' minimum standards governing their application are spelled out in the Trade Related Aspects of Intellectual Property (TRIPS) Agreement of the World Trade Organisation (WTO).

- 107 Intellectual property rights ensure a limited period of exclusive marketing rights to the holder. This exclusivity often enables the firm to charge prices above manufacturing costs. Competition is limited when a product is under patent, but might still be exerted by other substitute products. In addition, there are both high costs and large risks involved in investing in R&D for new products, and when new products come onto the market. This combination leads to high prices that make the latest health products too expensive for the poor, and therefore unaffordable for large numbers living in developing countries. Empirical evidence supports the theory that greater competition either in substitute or imitation products, or once off-patent from generic versions, leads to lower prices.
- 108 Recently, high-profile debate and campaigning by several non-governmental organisations has focused on maximising affordability of pharmaceutical products, and on finding the right balance between affordability and ensuring incentives exist for investment in research and development. The debate is largely about getting this balance right – rather than the principle of intellectual property protection *per se* - and the Articles, parameters and flexibilities within the TRIPs Agreement that affect this balance. The general debate about protection of intellectual property is even more intense when dealing with products that have such a significant impact on people's lives – such as access to the latest medicines in the poorest countries.
- 109 Both new products, and those currently available under patent, should be affordable to those that need them. In addition, as noted in Chapter 3, current global levels of research and development into new technologies for tackling HIV/AIDS, TB and malaria are too low to secure rapid progress towards more effective products needed to achieve large and sustained reductions in the disease burden. Therefore, there is *also* a need to ensure that there are adequate incentives for research and development into new and more effective health products for developing country markets.
- 110 The UK Government's view is that a minimum protection of intellectual property (as specified in the TRIPS Agreement) remains a necessary condition for R&D investments in new medicines, but in the case of these diseases, protection of intellectual property (IP) rights alone is *insufficient*. Research decisions are driven by the expected return on the investment – which includes the size of the market and the ability of the customer to pay.
- 111 It is therefore crucial that protection of IP goes hand-in-hand with the idea of a Global Fund for Health, and particularly the advance commitment to purchase new products. This requires partnership between governments and private producers – in which governments make a firm commitment to purchase new products, and the

- pharmaceutical industry boosts its activity to bring more effective products to the market and commits to sell them at a fair price.
- 112 While intellectual property protection needs to be sufficient to establish the right R&D incentives, sufficient flexibilities should be retained to ensure that patented products are available and affordable in cases of national emergency and where market power is abused. Such flexibilities are contained in the TRIPS Agreement, and more detail is given in the separate technical Appendix on intellectual property rights. However, without greater common international understanding on the interpretation of these flexibilities.
- 113 For example, ambiguity on what constitutes a “national emergency”, and on what terms normal patent protection should be suspended in these circumstances, could be substantially reduced. International agreement could also be established around the prevalence rate and/or rate of spread of a disease at which a national emergency is triggered. In the absence of significant clarification uncertainty is likely to lead to lengthy recourse to WTO dispute panels. The costs involved, likely delay and uncertainty of outcome all potentially serve to deter developing countries from making use of these flexibilities.
- 114 At the same time broad-based use of compulsory licensing provisions is likely to undermine the incentive for R&D and lead to downstream problems in ensuring that the right incentives are in place for the additional research into drugs and vaccines necessary for tackling the disease burden of developing countries. **For this reason, compulsory licensing should be used only as a policy measure of last resort** – where other efforts to address affordability such as increased international finance for product purchase and tiered pricing have failed.
- 115 While WTO dispute resolution panels will ultimately determine and hence define more precisely the interpretation of flexibilities under TRIPS, there is considerable confusion surrounding the circumstances that can allow the flexibilities within the Agreement to be used. The WTO should take the lead to ensure greater clarity on the spirit, and the letter, of the Agreement.
- 116 ***Recommendation:*** There is a strong case for the WTO TRIPS Council to seek to clarify the flexibilities available within the WTO TRIPS Agreement to help WTO members in achieving the Okinawa targets. This should involve consultation with a working group of developed and developing country governments, the private sector, and relevant multilateral and non-governmental organisations. These discussions should clarify the terms under which these flexibilities can be used, including ways in which voluntary licensing can be promoted (see next recommendation), and the circumstances in which, as a last resort, compulsory licensing can be invoked. This should be used as a first step to global agreement on interpretation. This will assist their appropriate use now, and limit lengthy, resource-consuming and uncertain recourse to WTO dispute settlement. The UK industry has already committed to a more

effective partnership to improve access to medicines in the report of the joint Pharmaceutical Industry Competitiveness Taskforce.

- 117 **Recommendation: We propose that this working group also considers ways in which voluntary licensing agreements between the pharmaceutical industry and developing countries can be made more widespread and more effective as a means of improving the affordability of health products for the poorest.** This proposal needs to be considered alongside our recommendation on a facilitative framework for tiered pricing, below, which would require action to prevent low-priced products intended for the poor in developing countries being imported instead to the developed world.
- 118 Finally, the UK Government has established a Commission to assess the impact on developing countries of the global minimum standards governing intellectual property protection covered in the Trade Related Aspects of Intellectual Property (TRIPS) Agreement. The Commission will consider how intellectual property rules might develop in the future in order to take greater account of the interests of developing countries and poor people.

Box 7.1: Compulsory and Voluntary Licensing provisions

Voluntary Licensing

Under voluntary licensing, either an application is made to the patent holder to gain a license or the patent holder approaches potential licensees to produce the patented product. This requires agreement between the licensee and the patent holder without prejudice to the rights of the patent holder.

Compulsory Licensing

Article 31 of the TRIPs agreement allows compulsory licensing and government use of a patent without the authorisation of its owner. This can only be done under a number of conditions aimed at protecting the legitimate interests of the right holder and paying compensation. The authority applying for a licence must have first attempted, unsuccessfully, to obtain a voluntary licence from the right holder on reasonable commercial terms, and adequate remuneration must be paid to the right holder. The authorisation granted under compulsory licensing must also meet certain requirements. In particular, it cannot be exclusive, and as a general rule is granted predominantly to supply the domestic market.

7.3 A framework for tiered pricing would help to improve affordability without weakening incentives ...

- 119 While a system that puts in place minimum standards of intellectual property helps to maintain incentives for research into health products, a tiered pricing system for such products should facilitate charging different prices in different markets. This should allow pharmaceutical companies to continue their pricing and marketing strategies in developed (or high price markets), and in addition, to sell at cost plus a smaller margin to the poor in developing countries (low price markets). Such a system, effectively implemented, thus offers a means of improving affordability of pharmaceutical products for the poorest while

not undermining incentives to invest in research and development on more effective future products.

- 120 According to economic theory, when tiered pricing is applied under certain monopoly conditions and effective separation can be achieved between price-sensitive markets, then tiered pricing (or in economic terms “Ramsey Pricing”) rules apply. In such conditions this is both economically efficient and equitable. In reality, tiered pricing will have the greatest benefits when the producer has a large share of the overall market, (i.e. there are few real substitutes) and where the markets can be clearly separated. Such conditions apply to many pharmaceutical products, and already seen pharmaceutical companies offer lower prices for anti-retroviral therapy to developing countries.
- 121 The operation of tiered pricing is however dependent upon the ability of the producer to segregate the markets in which different prices are charged. This is increasingly difficult with the trend increase in global trade, and reducing national barriers. But, without segregating markets, the lower priced products will tend to be traded at a mark up into higher price markets, sharing the value from the price differential between the middle traders and the end-high price consumer. This will erode the demand for the products at the high prices, and hence drive prices down and erode the overall profits of the pharmaceutical industry. Under these circumstances, pharmaceutical companies will have an incentive to adopt uniform pricing – which means higher prices for developing countries, and a reduction in overall consumer welfare.
- 122 ***Recommendation: We propose that support is given to this system of tiered pricing by putting in place a facilitative framework to ensure that low prices can be charged to the poor – without low-priced products being re-imported to higher price markets. This requires action both by producers – for example recognisable differential packaging – and by governments to ensure simple and effective trade regulation to prevent parallel importation. It also requires political will in developed countries, to accept that the poor in developing countries should pay less than home markets, and also in developing countries, to ensure that low price products reach the poorest and are not sold on to higher price markets.***
- 123 From an economic efficiency perspective, the more tiers linked to different prices and levels of development the better. Administratively however, the more complicated the system, the more difficult it will be to police any system and prevent parallel importation.
- 124 The UK supports the work of the European Commission to explore how such a system could be established. European Union markets already allow for no re-importation of cheaper patented products from outside the market. This could be achieved by different marketing of the low-price products to deter parallel imports. For a global system to work, wider developed world support, particularly from US and Japan would be needed. Such arrangement would also need to be discussed with pharmaceutical suppliers who stand to gain from larger markets in low

price countries, improved restriction of parallel importation across price tier boundaries and potentially lower transactions costs; but may face less flexibility in commercial arrangements.

- 125 Market segmentation within countries would also help efforts to have tiered pricing within countries between public and private markets. This will require political will, regulation and enforcement by developing country governments to ensure that the low price health products reach the poorest, without eroding higher price markets.
- 126 Such a system is unlikely to be applicable to all products. For many developing country diseases there are not clearly defined high and low price markets for the same health product, or there is a very small 'high price' market (limited mainly to travellers and ex-patriot workers). This includes tropical diseases such as TB and malaria, which limit the scope of tiered pricing. For tiered pricing to have a significant impact on access to health products for the poor, there needs to be a large enough market for the particular product in developed countries to allow the developer/producer to earn sufficient revenue to cover its R&D costs, plus an adequate return. A facilitative framework for tiered pricing will not be sufficient for price differentials on products for which effective demand in developing countries is small, and developed country markets too small to compensate.

7.4 Other measures can be deployed to improve affordability ...

- 127 It is worth stressing that tiered pricing is only one policy option and that there are additional factors that impact upon the price of health commodities to developing countries. First of all procurement policies are important, the need to have competitive tendering where possible, and transparent procedures. In addition a sound public procurement system encourages a more efficient and competitive economy, helps to reduce corruption and helps to provide value for money enabling public spending on health and education to reach more people more effectively.”⁺
- 128 Countries should also take advantage of bulk purchasing opportunities. National legislation is also often used to keep prices of pharmaceutical products low, while national taxes and tariffs can raise the price to consumers. At the country level, governments need to ensure that all national procurement, competition and industrial policies are conducive to getting the lowest possible price of health commodities.

Tax incentives for product donations

- 129 In the Budget (7 March 2001), the UK Chancellor of the Exchequer set out a new incentive to encourage the pharmaceutical industry to raise the level of donations of drugs and vaccines, and to do so in a more consistent manner, in support of developing countries' own health

⁺ UNCTAD Speech by Rt. Hon Clare Short MP, Secretary of State for International Development on Wednesday 16 February 2000

strategy and the needs of their people. Where drugs, vaccines and associated medical equipment are donated to designated international aid agencies and public health authorities, the value of the items donated will not be brought into charge to tax. Ancillary expenditure, such as distribution and transport costs, will be fully tax deductible.

7.5 Several measures strengthen incentives for research and development

- 130 Policy measures to strengthen incentives for research and development of new, more effective products can be broadly classified into three groups: “push”, “pull”, and regulatory measures:
- “Push” measures aim to stimulate research and development activity from an early stage in the product development timeline, for example through additional or better targeted R&D funding;
 - “Pull” measures aim to strengthen incentives for research and development by improving the prospective value of the market for producers of effective new health products, for example through a credible commitment to purchase effective new products as they become available in the future; and
 - Regulatory measures aim to speed up the international approval and licensing of effective new products, so that they might be made available more quickly to those that need them.

7.6 Targeted support is needed for research and development ...

- 131 The existing range of products to tackle HIV/AIDS, TB and malaria are not effective enough - nor sufficiently robust to new drug-resistant strains of the diseases - to offer a rapid, sustainable solution in preventing, diagnosing and treating these diseases. Vaccines to inoculate against HIV/AIDS and TB do not yet exist, and no long-term inoculation against malaria is available. The efficacy of many existing treatments is declining as drug-resistant strains of the diseases increase.
- 132 Despite the absence or decreasing efficacy of existing products, only 10% of global pharmaceutical R&D activity is targeted at the so-called “diseases of poverty”. This lack of action reflects the difficulties of research, the uncertain chances of success and the long timescale for developing effective new products. Targeted public support for research complements the policy options set out above to improve the affordability of existing health products and strengthen the incentives for private sector research and development by reducing the associated risks.
- 133 **Recommendation:** There should be additional carefully targeted public support for basic and applied research. This support for R&D should include innovative public-private partnerships to leverage private funds and expertise; support for the creation of a

clinical trials platform; and harmonisation of regulations to speed up approval and licensing of new, more effective products. Each of these components of support for R&D is summarised below and set out in more detail in Technical Annex 5.

Eligible diseases and products

- 134 ***Recommendation:*** To maintain an appropriate focus for additional public support for R&D, additional funds should, in the first instance, be restricted to activities related to new products to tackle HIV/AIDS, TB and malaria. This restriction should be subject to periodic review, with a view to later inclusion of research on products to tackle other diseases whose burden falls predominantly on the world's poorest people. It should be noted that the capability and capacity for research into these diseases is limited, and consideration should be given to developing the necessary capacity as part of additional public support.
- 135 ***Recommendation:*** products eligible for support should include vaccines, diagnostics, drug treatments, other as yet unknown products, and significant improvements to the efficacy of existing products.

Support for basic and applied research

- 136 Analysis by disease of available information on new products in the development "pipeline" indicates that although there are a handful of products in development to tackle HIV/AIDS and malaria, there is little activity on new products for TB. One likely reason for the activity on HIV/AIDS and malaria is that products for both diseases have developed country markets, albeit with different product requirements. When TB was all but eradicated in the developed world, priorities were refocused elsewhere.
- 137 There is a case for greater public support for basic and applied research on products to tackle the clades of HIV and strains of TB and malaria prevalent in developing countries. Support should be carefully targeted by disease to ensure that publicly-funded research does not crowd out private research. Instead, public funds should be used where possible to leverage additional private funds through innovative public-private partnerships. An alternative approach is for the public sector to fund and/or undertake basic research, handing emerging candidates over to the private sector for development. This approach was behind many of the existing anti-retroviral drugs used to treat HIV/AIDS.

Using existing mechanisms

- 138 Where possible, developed countries should aim to channel additional funds for appropriate research through existing mechanisms, to avoid creating new layers of bureaucracy. In some instances it might be necessary to extend existing eligibility criteria for national research funds to enable access by all institutions and researchers submitting

verifiably appropriate and credible applications, regardless of global location.

Public-private research partnerships

- 139 Recently, the shared desire of governments, non-governmental agencies, private companies and private foundations to combat infectious diseases has led to a proliferation of innovative public-private partnerships. These match expertise and funds in the public sector with those of the private sector. Substantial “new money” has been made available to researchers, including that from new philanthropists such as the Bill and Melinda Gates Foundation. The arrangements created to facilitate these new partnerships fall into two broad groups: ‘public sector programmes with private sector participation, operating under the auspices of intergovernmental agencies; and not-for-profit ‘public-private partnerships operating under the national laws of various countries’.
- 140 Examples of public-private partnerships to research and develop new products to tackle HIV/AIDS, TB and malaria include the International AIDS Vaccine Initiative, the Global Alliance for anti-TB Drug Development, and the Medicines for Malaria Venture (shown in the initiatives map in Chapter 4). ***Recommendation: public-private partnerships should be considered as a useful channel for additional public support, subject to appropriate governance and accountability structures, and monitoring of progress and outputs. Rationalisation of the proliferation of existing initiatives should be encouraged.***
- 141 Intellectual property issues are crucial in these PPP arrangements. Depending on the balance of funds and risk between the public and private partners, the need to ensure the right incentives for private sector to invest are weakened. Under such public-private partnership arrangements, the use of public funds should be used to ensure patent arrangements mean prices to the end consumer are affordable.

Tax incentives for R&D

- 142 Another approach is to use public funds to leverage private sector research and development activity. At the ‘International Action Against Child Poverty’ Conference in London on 26 February 2001, hosted by the Chancellor of the Exchequer and the Secretary of State for International Development, the UK announced that it would provide tax credits for research and development on drugs and vaccines for the diseases of poverty. The Chancellor set out his plans in the 2001 Budget on 7 March. The UK measures are summarised in Box 7.2. ***Recommendation: We recommend that other developed country governments consider adopting similar national tax measures to strengthen incentives to R&D for these diseases.***

Box 7.2: The UK's new Tax Credit for R&D to tackle the diseases of poverty

In his budget on 7 March 2001, Gordon Brown, Chancellor of the Exchequer announced consultation on a package of measures aimed at encouraging pharmaceutical and other companies to commit resources to the prevention and treatment of diseases primarily affecting people in developing countries, including a new drugs and vaccines tax credit. The measures are designed to encourage companies to increase their research effort on developing drugs and vaccines for the world's killer diseases.

Consultations are underway with interested parties on the design of a new vaccines tax credit to stimulate research into the development of vaccines and drugs to combat TB, malaria and those strains of HIV/AIDS that are prevalent in the developing world (the specified diseases) for legislation next year. The implementation and coverage of the credit will be decided on the basis of concrete commitments by the pharmaceutical industry to respond to the new incentives.

Companies undertaking research into the specified diseases will be eligible for an extra 50% relief on qualifying expenditure on top of existing relief's for R&D expenditure. This relief will compliment both existing R&D relief's and the general R&D tax credit for large companies about which consultation was announced in the budget.

Qualifying expenditure for the purposes of the new vaccines tax credit will be defined by reference to activities that fail to be treated as research and development in accordance with normal UK accounting practice and the guidelines on the definition of R&D published by the Secretary of State for Trade and Industry (based on the OECD Frascati Manual). The relief will be restricted to expenditure on the research and development of vaccines and drugs for the prevention and treatment of the specified diseases.

7.7 Establishing a clinical trials platform is key to reducing blockages in the R&D "pipeline" ...

- 143 Analysis by disease of products in the pipeline (Chapter 3) indicates a cluster of products in the stages prior to phase 3 clinical trials. Consultation with the pharmaceutical industry and public sector research institutions has revealed that the absence of an accessible clinical trials platform delays bringing new products through the later stages of testing and development, and might act as a disincentive to embark on basic research on new products.
- 144 Recognising this, and in the broader context of the European Commission's Programme of Action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction, the European Commission has proposed that a European Clinical Trials Platform be established to accelerate the development of new products for use in developing countries. The proposed clinical trials platform would facilitate networking and co-ordination of research; strengthen trials infrastructure in developing countries; and leverage funds to sponsor trials.

- 145 **Recommendation:** There is a strong case for the establishment of a clinical trials platform along the lines proposed by the EC, subject to agreement that developing countries would play a leading role in its development and operation; that trials would be restricted to products to tackle diseases of poverty in developing countries, with initial priority given to HIV/AIDS, TB and malaria. Access should be open to all appropriate products, without discrimination by global location or sector but with application of suitable user fees. It is important that work to establish a clinical trials platform – EC led or otherwise – begins soon, so that new products emerging in the near future can be appropriately trialled without delay.

7.8 Harmonising the regulation of new products can help to reduce delays in deploying effective new products

- 146 Before new products enter use, they are subject to rigorous regulatory scrutiny to assess safety, quality and efficacy. The regulatory process varies between countries by approach, criteria, standards, capabilities and timeliness. This variation causes delay in universal product availability as companies phase their efforts to gain approval in different jurisdictions and because additional effort is sometimes required to meet different scientific or dossier requirements.
- 147 **Recommendation:** appropriate human and financial resources be set aside to speed-up product approval by regulatory bodies in developed and developing countries, and harmonise the requirements imposed by developing countries.

Chapter 8: A call to action

- 148 The developing world faces a major health crisis that threatens to reverse decades of development gains. Three diseases - HIV/AIDS, TB and malaria - kill around 5.4 million people a year and have a debilitating effect on the 250 million people who suffer from them. The consequences for families are devastating: vital income is lost as ill health prevents work; children drop out of school to look after sick parents; and millions of children are orphaned every year. At the macroeconomic level, the burden of ill health and death significantly reduces economic growth and undermines efforts to reduce poverty. It is in everyone's interest to help defeat the major communicable diseases in developing countries, as they do not respect geographical or political borders. Globalisation and more international trade and travel have increased the opportunities for cross-border transmission of disease. Global warming is predicted to increase the number of malaria endemic countries.
- 149 Prevention, diagnoses and treatment of communicable diseases in developing countries requires affordable, effective health products (vaccines, diagnostics, drugs, condoms, bednets, etc.) to be available to those who need them. Public awareness and access to accurate information are also important. Many health products to tackle HIV/AIDS, TB and malaria are both unaffordable to those who need them and prone to decreasing efficacy in the face of multi-drug resistance and mutating strains of disease. Health systems in developing countries face severe capacity constraints that further undermine efforts to tackle the diseases.
- 150 Many existing initiatives to address HIV/AIDS, TB and malaria in developing countries support health care systems and sponsor or manage research into new, more effective health products. Our analysis and consultation showed that there is a clear need to increase support for improving health care systems and health promotion. It also showed that there are significant gaps in current activity, particularly relating to the affordability and effectiveness of relevant health products. The gaps include an absence of measures to address the:
- lack of effective demand for existing health products;
 - weak incentives for investment in research and development of new, more effective health products;
 - blockages in product development at the clinical trials stage;
 - regulatory delays for new health products; and
 - fragmentation of initiatives.
- These gaps seriously undermine efforts to defeat the diseases.
- 151 As stated in Chapter 5, the key issue for the international community is to agree action which will address the gaps identified. Chapters 6 and 7 of the report then set out some specific options for consideration which complement existing action and fill the gaps. They are intended to support and inform ongoing international discussions. The package is designed so that individual measures complement each other. For example, a clinical trials platform is unlikely to have a large impact on the burden of disease by itself. However, it

should enhance the effectiveness of the advance purchase commitment by addressing a bottleneck in the development process that the private sector cannot solve. This might accelerate the development of new health products considerably, perhaps by several years, enabling a significant reduction in the number of deaths and the prevalence of disease. Taken together, the measures offer a strong prospect of delivering rapid, substantial and sustainable reductions in the disease burden.

152 The challenge is immense and requires resources, expertise and commitment on a global scale. All members of the international community need to play their part and maximise their contribution to the shared agenda. Action is needed from a wide group of partners:

Developing country governments need to:

- demonstrate high-level political commitment to tackling HIV/AIDS, TB and malaria; and assess their budget priorities within the context of agreed poverty reduction strategies, with appropriate resources allocated to health;
- ensure that resources allocated to health are efficiently and effectively deployed, according to national health sector strategies;
- enable the private sector to maximise its contribution in providing health care, including the distribution and delivery of health products;
- play an active role in designing and managing a Global Fund for Health;
- explore the possibility of collaborating with regional partners to take advantage of bulk purchasing of health products;
- review tax and tariff levies on pharmaceutical and other health products;
- facilitate tiered pricing of health products by putting in place appropriate export controls;
- play a leading role in the development and operation of a clinical trials platform; and
- work together to harmonise the regulatory process and approval of new health products.

Developed country governments need to:

- commit additional financial and technical resources to support national health sector strategies in developing countries, paying particular attention to sustainable improvement and expansion of health care systems;
- commit additional financial resources to a Global Fund for Health; and credible arrangements for resourcing an advance purchase commitment;
- facilitate tiered pricing of health products by putting in place appropriate import controls;
- consider introducing or increasing tax relief on donations of appropriate health products;
- increase support for basic and applied research into the strains of HIV/AIDS, TB and malaria prevalent in developing countries;

- provide additional support for public-private research partnerships, and work to rationalise the proliferation of existing public-private research initiatives;
- consider introducing or increasing tax relief on research and development on relevant health products;
- support the development and operation of a clinical trials platform; and
- work together to harmonise the regulatory process and approval of new health products.

Multilateral and international financial institutions need to:

- commit financial and/or technical resources to support national health sector strategies in developing countries, playing to their relative advantages and strengths; and
- commit financial and/or technical resources to a Global Fund for Health, including assistance with banking and fiduciary functions, procurement and monitoring progress.

Civil society in developed and developing countries needs to:

- work with governments to reach the shared goals of improving health outcomes, through a range of activities including financial and technical support, advocacy and awareness-raising.

The global **pharmaceutical industry** needs to:

- commit substantial new resources to research and development for new, more effective products which can make a major contribution to the fight against HIV/AIDS, TB and malaria;
- contribute to the Global Fund for Health, whether financially or in product donations;
- respond to new incentives such as the UK's tax credit to increase product donations which support developing countries own health strategies and are sustained;
- play a constructive role in discussions to clarify how flexibilities in the TRIPS agreement can be used to improve the affordability and effects of their products in developing countries, supporting a more flexible approach to TRIPS where this will make a real difference to health outcomes;
- maintain a dialogue with developing countries facing health crises to reach agreement on ways in which affordability of health products can be improved;
- work with developing countries and others to expand the use of voluntary licensing agreements for appropriate local production of products under patent, and to identify how such agreements can have a larger impact on the affordability of their products and their impact on the disease burden; and
- expand the use of tiered pricing, working with governments and others to establish a framework to facilitate this.

- 153 The UK is playing a major role in stimulating a greater and better co-ordinated international effort to tackle communicable diseases in the developing world. UK activity includes:
- high-level political commitment to the creation of a Global Fund for Health;
 - financial and technical support to developing countries for the improvement and expansion of their health systems. Since 1997, the UK Department for International Development has committed £1 billion to building primary health care systems;
 - tax credits to encourage the pharmaceutical industry to raise the level of donations of drugs and vaccines, and to do so in a more consistent manner, in support of developing countries' own health strategies and the needs of their people;
 - tax credits for research and development on drugs and vaccines for the diseases of poverty; and
 - financial support for public-private partnerships, such as the Global Alliance for Vaccines and Immunisation (GAVI).

174 As well as the package of measures in this report, a concurrent monitoring and evaluation system should be set up, with an independently prepared, publicly available report made available to the UN Secretary-General in 2005.

175 The convergence of the development, finance, trade and foreign affairs agendas has opened a window of opportunity for the international community to act together to make real difference in tackling communicable diseases of the poor, particularly HIV/AIDS, TB and malaria. The time to act is now.

The UK is actively engaged in discussions on these key areas with our international partners. We would welcome comments on the proposals contained in this report, which should be addressed to:

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Comments can also be sent by e-mail to:
global.health@cabinet-office.x.gsi.gov.uk

References

1. UK Government (1997) *Eliminating World Poverty: A challenge for the 21st Century*. Command Paper 3789. TSO: London.
2. DFID (2000) *Better Health for Poor People: Strategies for achieving the International Development Targets*. DFID: London.
3. UK Government (2000) *Eliminating World Poverty: Making globalisation work for the poor*. Command Paper 5006. TSO: London.
4. Phillips DR (1990) *Health and Health Care in the Third World*. Longman: UK
5. Barrera A (1990) The role of maternal schooling and its interaction with public health programs in child health protection. *Journal of Development Economics* 32.
6. World Education Forum (2000) *The Dakar Framework for Action. Education for All: Meeting Our Collective Commitments*.
7. DFID (2001) *The challenge of universal primary education*.
8. DFID (2001) *Achieving Sustainability: Poverty Elimination and the Environment. Strategies for achieving the International Development Targets*. DFID: London.
9. World Bank (1993) *World Development Report 1993: Investing in Health*. Oxford University Press: New York.
10. Gwatkin D and Guillot M (2000) *The Burden of Disease among the Global Poor – current situation, future trends, and implications for strategy*.
11. WHO (2000) *World Health Report 2000: Health systems – improving performance*. WHO: Geneva.
12. Source: UNAIDS
13. Hunter S and Williamson J (2000) *Children on the Brink*. USAID: Washington.
14. Gallup JL and Sachs JD (1999) *Malaria, Climate, and Poverty*. Consulting Addistance on Economic Reform II discussion paper 48.
15. Source: Initiative on Public-Private Partnerships for Health
16. Global Forum for Health Research (2000) *The 10/90 Report on Health Research*. World Bank: Washington.
17. Smith S (2001) *Current Global Expenditure on malaria, tuberculosis, and HIV/AIDS*. Report produced for the PIU by the Department of Public Health and Policy, London School of Hygiene and Tropical Medicine: London.
18. Kumaranayake L, Kurowski C, Conteh L, Watts C (2001). *The Costs of scaling up priority health interventions for low-income countries: preliminary results*. Commission on Macroeconomics and Health, Working Group 5 Draft Working Paper Number 19.
19. DFID (1999) *Prevention Works: Uganda, Senegal and Thailand – Blair announces support for HIV/AIDS in the developing world*. Press Notice 12th November 1999.
20. UK Government (2001) *Forging a New Commitment: Tackling the Diseases of Poverty*. Consultation Paper for the Conference on International Action Against Child Poverty – Meeting the 2015 Targets. 26th February 2001.
21. Source: Stop TB
22. Danzon P (1998) *The Economics of Parallel Trade Review Article*, *Pharmaeconomics*
23. HM Treasury (2001) *Budget 2001 – Investing for the Long Term: Building Opportunity and Prosperity for All*.
24. Widdus R, Chacko S, Holm K, Currat L (2001) *Towards better defining 'public private partnerships' for health*. Global Forum for Health Research: Geneva.
25. Isbell M and Widdus R (2001) *Actions to avoid regulatory delays for vaccines against HIV/AIDS*. IAVI



Annexes to Tackling the diseases of poverty

**Meeting the Okinawa/Millennium targets for
HIV/AIDS, tuberculosis, and malaria**



**Performance and Innovation Unit, Cabinet
Office, London.**

8 May 2001

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Annex 1: Health section of the G8 communiqué – Okinawa July 2000

- 1 Health is key to prosperity. Good health contributes directly to economic growth whilst poor health drives poverty. Infectious and parasitic diseases, most notably HIV/AIDS, TB and malaria, as well as childhood diseases and common infections, threaten to reverse decades of development and to rob an entire generation of hope for a better future. Only through sustained action and coherent international co-operation to fully mobilise new and existing medical, technical and financial resources, can we strengthen health delivery systems and reach beyond traditional approaches to break the vicious cycle of disease and poverty.
- 2 We have committed substantial resources to fighting infectious and parasitic diseases. As a result, together with the international community, we have successfully arrived at the final stage of polio and guinea worm eradication, and have begun to control onchocerciasis.
- 3 But we must go much further and we believe that the conditions are right for a step change in international health outcomes. We have widespread agreement on what the priority diseases are and basic technologies to tackle much of the health burden are in place. In addition there is growing political leadership and recognition in the most afflicted countries that health is central to economic development. We particularly welcome the success of the recent HIV/AIDS conference held in Durban and the importance attached to tackling HIV/AIDS by African leaders, donors, international financial institutions and the private sector.
- 4 We therefore commit ourselves to working in strengthened partnership with governments, the World Health Organisation (WHO) and other international organisations, industry (notably pharmaceutical companies), academic institutions, NGOs and other relevant actors in civil society to deliver three critical UN targets:
 - Reduce the number of HIV/AIDS-infected young people by 25% by 2010.
 - Reduce TB deaths and prevalence of the disease by 50% by 2010.
 - Reduce the burden of disease associated with malaria by 50% by 2010.
- 5 In order to achieve this ambitious agenda our partnership must aim to cover:
 - Mobilising additional resources ourselves, and calling on the MDBs to expand their own assistance to the maximum extent possible;
 - Giving priority to the development of equitable and effective health systems, expanded immunisation, nutrition and micro-nutrients and the prevention and treatment of infectious diseases;
 - Promoting political leadership through enhanced high-level dialogue designed to raise public awareness in the affected countries;
 - Committing to support innovative partnerships, including with the NGOs, the private sector and multilateral organisations;

- Working to make existing cost-effective interventions, including key drugs, vaccines, treatments and preventive measures more universally available and affordable in developing countries;
- Addressing the complex issue of access to medicines in developing countries, and assessing obstacles being faced by developing countries in that regard;
- Strengthening co-operation in the area of basic research and development on new drugs, vaccines and other international public health goods.

6 We note with encouragement new commitments in these areas. We strongly welcome the World Bank's commitment to triple International Development Association (IDA) financing for HIV/AIDS, malaria, and TB. We also welcome the announcements to expand assistance in this area made by bilateral donors.

7 In addition, we will convene a conference in the autumn this year in Japan to deliver agreement on a new strategy to harness our commitments. The conference should look to define the operations of this new partnership, the areas of priority and the timetable for action. Participation of developing country partners and other stakeholders will be essential. We will take stock of progress at the Genoa Summit next year and will also work with the UN to organise a conference in 2001 focusing on strategies to facilitate access to AIDS treatment and care.

The full Communiqué can be read at:

<http://www.mofa.go.jp/policy/economy/summit/2000/communique.html>

Annex 2: A global fund for health, and an advance purchase commitment

Introduction

Chapter 6 set out that a Global Fund for Health could reduce the burden of diseases in the poorest countries by:

- making existing products (drugs, vaccines and other products) available to the poorest countries; and
- creating incentives for new, more effective products to be developed by guaranteeing that they will be purchased.

This Annex proposes:

- principles to underpin a Global Fund for Health
- specification options for the purchase of existing products
- specification options for an advance purchase commitment
- functions and possible models for the governance and operation of the Fund

Section 1: Principles of a Global Health Fund

- 8 The Fund should be underpinned by a number of principles agreed by the international community. Draft principles, based on the principles developed and agreed at the Okinawa International Conference on Infectious Diseases (December 2000) are:
- early inclusion of developing countries to ensure their full involvement in design and participation in the governance of the Fund. Products purchased through the Fund should be in response to developing countries' requests, be suitable for delivery in developing countries and be cost-effective;
 - a light governance structure that encourages drive and leadership, keeps decision-making close to developing countries and enables them to play a major role in governing the Fund, be involved in resource allocation decisions, and monitor health improvements;
 - to support and build on existing country-led health strategies and integrate with broader development processes, including Poverty reduction strategies and sector wide approaches. The planning burden and transaction costs to developing countries should be minimal;
 - to be a truly global partnership – drawing in donations from governments, foundations and the private sector. It should not rely on or be dominated by any one funder. It should be transparent, driven by the need to deliver better health outcomes, and governed by principles supported by all;
 - making products available and affordable to all those that need them. The Fund should not provide support for health systems. Instead health

systems should be strengthened through existing health sector programmes to enable products to be delivered;

- focusing first on the poorest countries with the highest burden of disease and setting out clear conditions for eligibility;
- sustainability through a long-term commitment to tackle diseases in developing countries;
- lesson-learning to facilitate rapid implementation and scaling-up responses to the diseases, through effective evaluation and peer review, so the effectiveness of strategies can be improved rapidly; and
- promote co-ordination of product provision to developing countries.

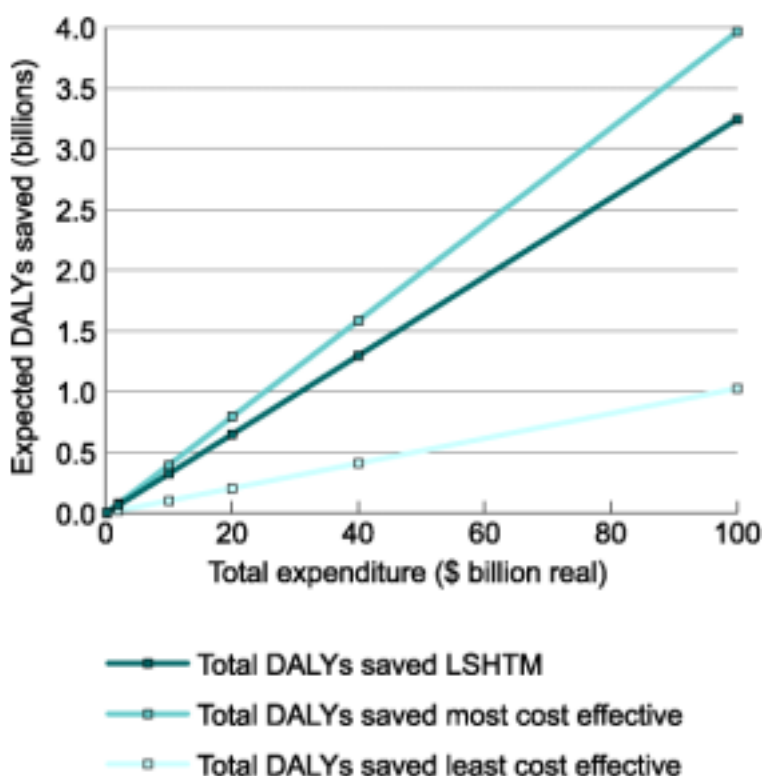
9 In developing proposals for a Global Fund for Health the international community will need to consider a range of issues for specification. These should be developed through a process of consultation with all key stakeholders including developing countries. Set out below are our preliminary views on how a Global Fund for Health could be specified.

Section 2: Current purchase

Resource requirements

10 A Global Fund for Health would need to be big enough to have a real impact in tackling communicable diseases, in particular HIV/AIDS, TB and malaria. It would need to increase incrementally as developing countries' capacity increases. Early indications suggest that a substantial scaling-up – of the order of \$billions per annum – is required. Figure 1 illustrates the expected impact over 20 years of different sizes of the Fund, derived from our modelling in annex 6.

Figure 1: Expected DALYs saved by a Global Fund for Health



Section 3: Eligible diseases

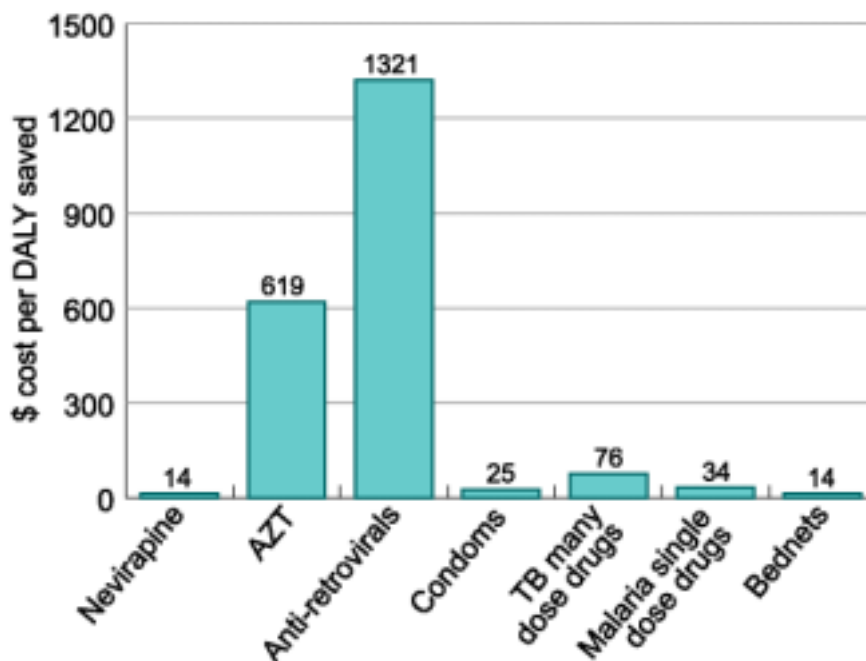
- 11 Chapter 2 set out that communicable diseases are a major killer of poor people in developing countries. A Global Fund for Health should focus on communicable diseases, in particular on HIV/AIDS, TB, and malaria, and childhood communicable diseases. In addition to being major killers, these diseases are where availability of effective products could make a major difference to health outcomes.

Section 4: Eligible expenditure

- 12 A Global Fund for Health should focus on adding value where there is a clear gap in existing action. It should focus on making products available to those that need them but cannot currently afford them. It should focus on purchasing health products that are cost-effective, appropriate for delivery in, and requested by, developing countries. Eligible products should include not only treatment drugs but also other products vital for prevention, and diagnosis, such as condoms, HIV testing kits and simple diagnostics. Our analysis suggests that the mix of products purchased will determine the number of DALYs saved for a given size of Fund. Figure 2 shows the result of cost-effectiveness modelling of different health products.
- 13 Preventive products such as bednets and condoms are very cost-effective, suggesting that a large proportion of the Fund should be spent on preventative health products. Treatment will also be required and is appropriate and cost effective as part of the prevention and care continuum of common communicable diseases such as malaria and TB. Treatment of communicable

disease reduces transmission to healthy individuals, and in the case of sexually transmitted diseases, is a cornerstone of HIV prevention strategies. Only treatments that are suitable for delivery in developing countries and are cost-effective should be purchased by the Fund.

Figure 2: Relative cost-effectiveness of existing health products



- 14 GAVI meets most existing vaccine requirements. National budgets and bilateral programmes meet other routine vaccine needs. However the Fund could provide finance to top up existing provision if necessary and finance future new vaccines to tackle HIV, TB or malaria. It could channel resources through existing mechanisms such as GAVI, where appropriate.

Section 5: Prices

- 15 A Global Fund for Health would be in a strong position to negotiate reasonable prices for bulk purchase of health products and should follow best-practice in procurement, ensuring as far as possible competitive, fair, open and transparent procedures.

Section 6: Advance purchase commitment

- 16 An advance purchase commitment within the Global Fund for Health could provide an effective incentive for research and development (R&D) by ensuring that there is a market for the new products needed. To be an effective incentive for R&D, this commitment must be credible and must represent a commitment of resources beyond the annual budget for purchase of existing products.
- 17 Estimates from our model suggest that an advance purchase commitment is the most cost-effective means of encouraging the development of new products. No resources would be spent under an advance purchase commitment until more effective products are available.

Resource requirements

18 The advance purchase commitment must be large enough to act as a sufficient incentive for firms to undertake R&D. There is no clear evidence of the size of market needed to incentivise R&D. Estimates of necessary annual market size per product range from \$100 million to \$500 million. Above the minimum size, the larger the commitment, the greater the level of R&D, the earlier new commodities are likely to be developed, and the higher the number of DALYs saved. Figure 3 shows the expected additional DALYs saved by an advance purchase commitment. Figure 4 shows the estimated median time of arrival of new health products.

Figure 3: Expected additional DALYs saved by an advance purchase commitment

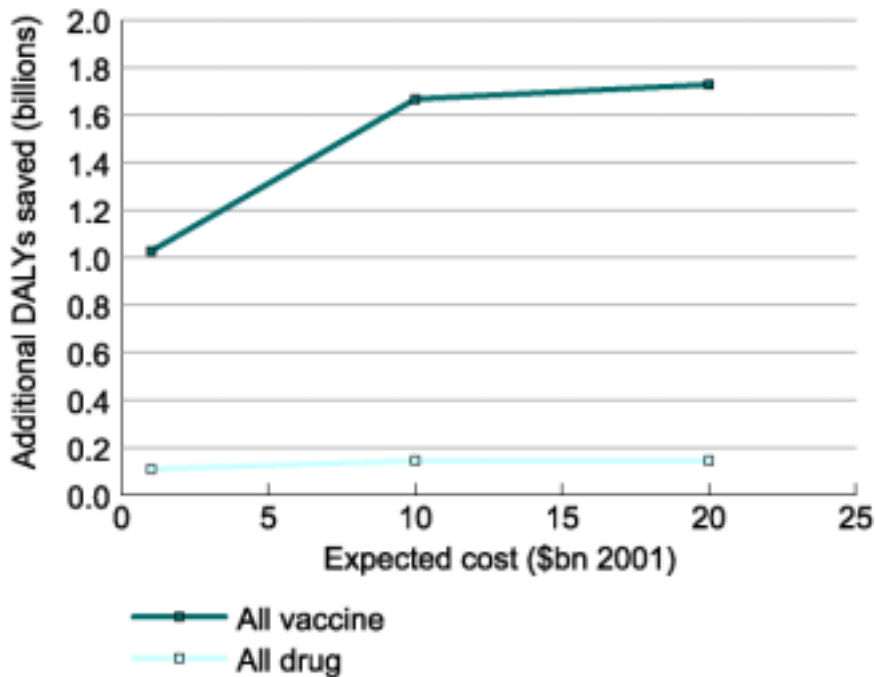
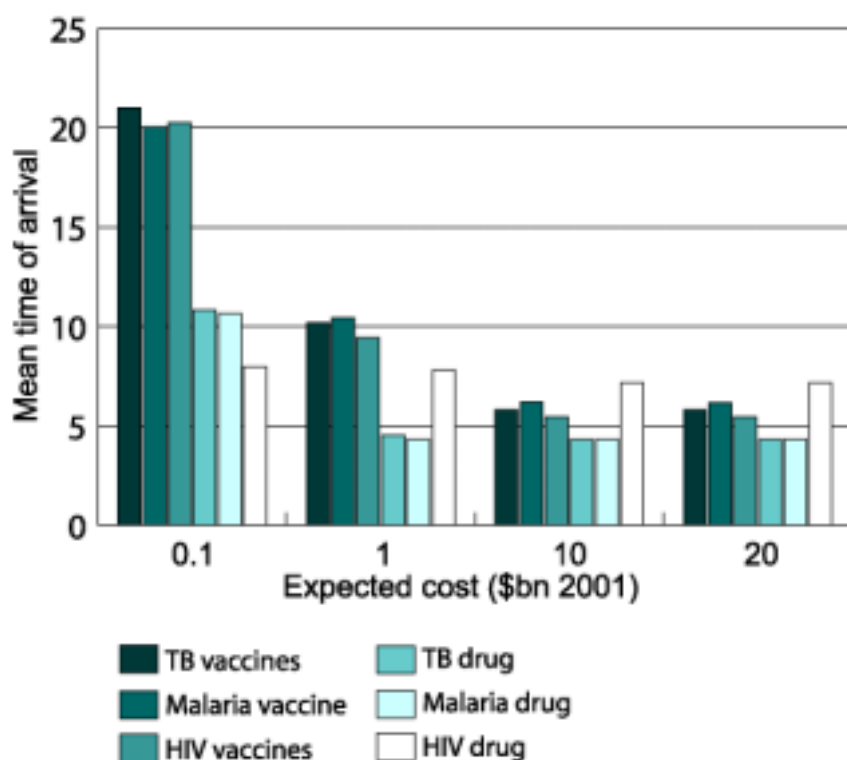


Figure 4: Estimated median time of arrival of new health products



Section 7: Eligible diseases and expenditure

- 19 To be credible the commitment must clearly state:
- which diseases it will purchase new products for; and
 - the specific products that it will purchase.
- 20 As the main report sets out, there is a clear rationale for focusing initially on HIV/AIDS, TB and malaria. To provide clear incentives it may be necessary to specify in advance the proportion of the commitment that will be dedicated to each disease. Our analysis indicates that a commitment to purchase new vaccines will have the greatest impact. However, drugs are also necessary for treating those already infected. Treatment of those infected can also reduce new infections.
- 21 In the absence of sufficient resources to provide an incentive for more than one disease, the advance purchase commitment could cover only one disease or one type of product. Decisions on which diseases/products to cover would need to be made by the governing body.
- 22 Eligible products would need to:
- meet normal safety specifications, such as approval by regulatory bodies;
 - be cost-effective with an expected impact on health outcomes significantly above existing products; and
 - be requested by a developing country.
- 23 The commitment would be activated when an eligible product became available. Products purchased by the commitment should be driven by the

demands of developing countries. Developing countries should be made aware by the Fund of new products that have reached market and are effective enough to be eligible for support through the advance purchase commitment. The products purchased (and the relative proportions of products purchased where there is more than one new product) should be determined by developing country requests.

Section 8: Price

- 24 Firms need to be sure that once they have produced a product they will be able to receive a price for it that will enable them to recoup their costs. This may be a particular concern as firms may anticipate that the Global Fund for Health will use its power as a monopsony purchaser to drive down prices to marginal cost once the product has been developed (the firm would then be unable to recoup R&D costs unless in a higher priced market).
- 25 One option would be to commit in advance to the price the Fund will pay for a certain product and the quantity it will purchase. However, this is highly risky given how little is known about future needs, the efficacy of future products, or R&D costs. It could commit to a price that is too high (the Fund pays more than it needs to) or too low (the commitment does not act as an incentive).
- 26 Instead of specifying price and quantity in advance, a better option might be a commitment to paying prices that will enable firms to recoup their costs and be adequately compensated for the risk of failure that they assumed during development. In addition the commitment could specify the total \$ per person immunised/treated that the commitment would pay. This would provide firms with an indication of the returns they will receive on their investment. Alternatively, the advance purchase commitment could be used to purchase the patent on a new product.

Section 9: Governance and operations

Eligible recipients

- 27 The Fund should be for those most in need. This will enable it to have the greatest impact. It should focus first on the poorest countries with the highest burden of disease. To ensure that products provided by the Fund reach those in need, eligible countries should:
 - show high-level political commitment to reducing communicable diseases, particularly HIV/AIDS, TB and malaria. This commitment should be reflected in national health strategies; and
 - have a health care system capable of delivering the products provided through the Fund to those who most need them.
- 28 Clear benchmarks could be put in place for assessing countries' readiness through their poverty reduction strategies. Multilateral and bilateral donors should prioritise support for poor countries with weak delivery systems through their existing health sector programmes to enable these countries to become eligible for the Fund.

Contributors

- 29 The Fund should be a truly global partnership – drawing in donations from governments, not-for-profit organisations and Foundations. Foundations are already very active in this area and the Fund should welcome their continued presence. The wider private sector could also be a source of potential donations to the Fund and ways of involving the private sector in developed and developing countries should be explored.

Governance

- 30 The Fund should maximise use of existing national systems and processes, including the Poverty Reduction Strategy process. National policies and priorities should be supported. In setting in place the governance structures of the Fund, the international community should draw on and learn from the experiences of setting up other international initiatives, for example the Global Environmental Facility and the Global Alliance for Vaccines Initiative.
- 31 There is a range of complex issues that need to be addressed in setting in place appropriate governance structures. A variety of governance models could be adopted for the Global Fund for Health. Decisions on which model to adopt is for the international community and should be decided through consultation with key players (including recipients, funders, private foundations, UN agencies and the World Bank).
- 32 Governance should be kept as light as possible, with decision-making kept close to developing countries. Functions to be undertaken under any governance model might include a governing body/Executive Board representing key stakeholders, effective administration and country level mechanisms:
- a small, high level **Executive Board** of key stakeholders, including representatives of recipients, funders and multilateral agencies, which might:
 - set a long-term vision and strategy;
 - make decisions on resource allocation;
 - monitor and evaluate the effectiveness of the Fund; and
 - provide accountability to funders for resources invested and to recipients for actions undertaken through the Fund.
 - a small **Secretariat** to support and report to the Executive Board, which might:
 - oversee procurement;
 - implement Executive Board decisions;
 - provide administrative structures that ensure proper use of Funds;
 - oversee monitoring and evaluation of Funds dispersed; and
 - provide technical advice to the governing body, especially on resource allocation.
 - **country level mechanisms** which might include:

- appraising need and developing requests for support as part of the process of national health strategies and Poverty Reduction Strategies;
- planning for delivery; and
- monitoring health outcomes as a result of products provided through the Fund.

33 In addition to these functions a Global Fund for Health could play a strong role as an advocate on the international stage for those suffering from these diseases. It could ensure their voices are heard and negotiate on their behalf. The size of the Fund and the high level commitment from a wide range of funders would ensure it had a strong voice.

Section 10: Operational Modality

Accessing the Funds

34 Developing countries need to be able to access funds in a way that minimises additional planning burdens. Assessment of need for resources from the Fund should take place as part of the existing process of country level health strategies. Requests put to the Fund should clearly link into and form part of existing strategies at country or sector level (e.g. Poverty Reduction Strategies). The Executive Board would review the requests and make decisions about relative priorities. A clear criteria for deciding resource allocation should be developed in line with the principles set out earlier in this annex.

Dispersing resources

35 Resources need to be dispersed to countries in the most efficient way that minimises transaction costs and opportunities for fraud. Options include directly purchasing products to meet developing countries' requests. This would enable the Fund to utilise its purchasing power to negotiate reasonable prices.

Section 11: The role of International Development Association (IDA) Loans

36 IDA is well placed to help facilitate the link a Global Fund for Health and development programmes at the country level, through the over-arching framework of the Poverty Reduction Strategy process. IDA exists to support country programmes, including lending, analytical and advisory work, and capacity building. It is already active in the health sector in many developing countries and plays a major role in financing and facilitating the building of primary health care systems, which are essential for the delivery of health products to poor people.

37 As part of its country-based programmes, IDA could be involved in financing the purchase of health products. How far IDA financing should be formally integrated with a Global Fund for Health would depend on the final scope, financing arrangements and governance of the Fund. Technical problems – as

well as problems of principle – in formally earmarking IDA funds for a Global Fund for Health, or in IDA undertaking contingent liabilities, would be difficult to overcome. More importantly, IDA would not provide additionality in wider development finance; a formal commitment to a Global Fund for Health would be at the expense of other development priorities.

Section 12: Co-ordination of international initiatives

- 38 There are currently a range of existing initiatives for addressing communicable diseases in developing countries, particularly HIV/AIDS, TB and malaria. However, most of these initiatives do not provide access to products. A Global Fund for Health should improve co-ordination by:
- providing a clear mechanism for funding product provision to developing countries. Donors can contribute to the Fund rather than setting up separate initiative; and
 - encouraging existing multilateral initiatives that provide health products to developing countries to become part of the Fund where appropriate and working with them where a separate focus is needed or where existing arrangements are effective (e.g. GAVI).

Annex 3: The impact of intellectual property rights on access to health products

Introduction

1 There has been a growing public interest in the impact of intellectual property protection on the price of medicines and treatment of diseases in the developing world. While the majority of essential medicines needed by the poor are no longer under patent protection, there are some that are (including medicines to tackle drug resistance, HIV opportunistic infections and anti-retroviral therapy), and any new drug or vaccine to come onto the market will be. Particularly high profile has been the debate about access to anti-retroviral therapy, and the high prices charged by the Western pharmaceutical companies for their patented products compared to the price of locally produced imitation versions by others, such as Indian, Brazilian and Thai companies.

2 In Sections 1 and 2, this annex explores the theory and empirical evidence behind the question: Does intellectual property protection mean more research in new drugs? Or that drugs are too expensive for the poor? Section 3 will explore the issue of affordable HIV drugs and anti-retroviral therapy and Section 4 will consider other issues affecting the prices of medicines. Finally, Section 5 considers the policy options open to governments and the international community to lower the prices of patented medicines. In the next annex the related issues of differential pricing and parallel trade are explored separately, as one possible policy measure to assist in keeping prices lower for those that cannot afford them, and need them most.

Section 1: Intellectual property protection: the theoretical arguments and the current situation

The theory

- 3 As discussed in the Working Paper on *The Rationale for Government Intervention*, with no policy intervention firms will not invest the social optimum in new research. Without regulation to prevent it, once a new invention becomes publicly available, competitors will be free to reproduce it. As a competitor only needs to make a return on the manufacturing costs of the product, it will be able to undercut the original inventor, who is trying to sell their product at a price that makes a return on both manufacturing *and* research and development costs. Under free competition, the inventor will lose market share to its competitors, be forced to lower prices and not make an adequate return to justify the total funds invested. The inventor will realise this at the outset, and will therefore not invest in research and development, despite the fact that there is demand for and social benefits from the new technology.
- 4 Protection of intellectual property is a policy response to correct this market failure. Patents are part of a broader system of intellectual property that

includes copyright, trademarks, and protection of trade secrets. Patents are granted if the inventor can demonstrate: novelty, an inventive step, and capacity for industrial application. A patent can be filed on either a process or a product. By allowing the inventor the *exclusive* rights to market the product over a temporary period, the inventor can market their product at a price that maximises the return on their total investment, with limited competition⁺. This system of patent protection thus provides an incentive to encourage firms to undertake new research.

- 5 The patent system corrects for the market failure deterring research and development, but creates a new market failure. With an exclusive licence, the firm faces limited competition. As with any monopoly or quasi-monopoly, this will lead to higher prices than justified by the necessary recouping of research and manufacturing costs, and lower consumption, than would be socially optimal. It is this that is underpinning the public debate on patented HIV drugs and anti-retroviral therapy, which we discuss in Section 3. In short the debate is about getting the balance right between a system that puts in place the right incentives for R&D, but does not give excessive power to the patent holder that results in unjustified high prices over many years.
- 6 From a social welfare perspective, an optimal system would be one where the firm was compensated for the funds invested in the research – but once compensated, products are sold to consumers at manufacturing cost. Government or public purchase of the patent, and then placing the new knowledge in the public domain, is considered as a policy option in Section 4.
- 7 The economic arguments, played out above with products and consumers as an example, also apply to ideas and new technology more generally and their availability to firms and governments.
- 8 In short, the theory behind patent protection is therefore to put in place the right *incentives* for research and development (R&D) of new products. However, patent protection may be necessary* but of itself is not sufficient to encourage R&D. The Board of any firm is ultimately concerned about the return to shareholders, and the overall expectation about the profit to be made on the investment. Therefore, additional factors taken into account include the probability of success, the size of the market and the willingness and ability of consumers to pay for new products. These additional factors are obviously critical when examining the incentives for R&D in diseases that affect large numbers of very poor people, and where the science is simply not easy to crack. While important, patent protection is not the only, and arguably not the most significant, factor influencing R&D investment in the key diseases of HIV/AIDs, TB and Malaria.
- 9 There is an opportunity cost to funds spent on R&D, and typically the decision to invest in one product or another, is based not solely on which will make a profit, but which will make the bigger return on investment. Therefore, not

+ Competition is limited in the sense that there are limitations on using the intellectual property to produce a similar product, but they may face competition from substitute goods.

* This could apply to consumers or others, e.g. other companies and firms may also want to purchase the new technology. In reality, the patent itself has an economic value, as a licence to use the technology can be sold to others. This is known as voluntary licensing.

every potentially profitable research opportunity will be pursued. This is relevant in the case of drugs for developing countries where the returns – even when positive – are unlikely to be in the same league as returns on the most popular products in developed countries.

- 10 The macroeconomic implications of intellectual property protection are that if firms invest more in R&D, this adds to a country's overall competitiveness and comparative advantage. While not sufficient in and of itself, intellectual property protection is likely to encourage both domestic investment and foreign investment suggesting possible increased foreign direct investment (FDI) and trade prospects. In addition there are possible spillover effects to local production from both FDI, and public disclosure of new research. Both of these can be expected to result in better economic prospects and sustainable growth. New technology, knowledge and ideas are important in determining a country's comparative advantage.
- 11 However, it is difficult to know how changes to a country's intellectual property regime are going to impact upon their trade prospects, particularly for those whose current comparative advantage is in imitating or counterfeit products. Once copying becomes inconsistent with their national legislation, there is an argument that they will no longer be able to exploit this opportunity to "catch-up" with developed economies.

The current situation

- 12 Until 1995, protection of intellectual property was a matter of national legislation. Since then global *minimum* standards of intellectual property, including patents, are covered in the Trade-Related Aspects of Intellectual Property (TRIPS) Agreement, with which all World Trade Organisation (WTO) members governments have committed themselves to comply must comply. The period of exclusivity for the patent holder is specified as twenty years from the date at which the patent is registered. Given the length of time taken to develop and approve a pharmaceutical product, this implies an exclusive marketing period of between 8 to 15 years on average. Disputes on the application of the TRIPS agreement, are subject to WTO Disputes Settlement. The main elements of the TRIPS Agreement that are relevant to the health debate are explained in the WTO's TRIPS and Pharmaceuticals factsheet*. In addition to TRIPS's minimum requirements, individual WTO Member States are free to maintain and expand their existing IP regimes.
- 13 Developing countries had five years until 2000 to implement TRIPS (Art 65.2). In technological sectors where there was no previous patent legislation accorded, developing countries have until 2005 (Art 65.4). Least developed countries have until 2006 and they can apply for subsequent extensions beyond this date. According to the WTO Secretariat I 1995, in only 13 countries, patent protection under national legislation did not then include pharmaceuticals. Therefore complying with TRIPS represents a global strengthening of intellectual property protection for medicines in a few countries. It is important to distinguish between the least developed and poorest countries, and those developing countries that are both more developed economically and have developed their own capacity for producing

* http://www.wto.org/english/tratop_e/trips_e/tripsfactsheet_pharma.pdf

pharmaceuticals. This latter small group has the ability to supply their domestic market with imitation products and to export them legally. But rights of patent holders and the legal ambiguities surrounding importing imitation products mean that the majority of developing countries without their own indigenous pharmaceutical industry face even greater problems of access to patented health products because of their relative cost.

- 14 During the period of marketing exclusivity, companies are able to protect their product from competition in those countries where the patent is recognised. However, during the transition period prior to the full implementation of TRIPS, some countries do not yet recognise patents on products, and are therefore able to imitate patented products by re-engineering them. The most well publicised cases are from the Indian pharmaceutical industry who are able to produce versions of Western products such as anti-retrovirals and Viagra at a fraction of the price they are sold for in the West.

The critics

- 15 The current system of intellectual property protection as represented by the TRIPS Agreement has received a range of criticisms. On the one hand they suggest that the balance between incentives for research and innovation and affordability is not optimal, and on the other that the current system has high transaction costs and creates insufficient incentives for original research.
- 16 Intellectual property protection itself may not provide socially optimal incentives for research. If the social value of the invention is actually much larger than the private value, then firms taking decisions to invest in R&D based on what the private customer will pay, will not be socially optimal.* Kremer points to evidence that suggests that this is the case and that on average the social value may be at least twice the private value. Furthermore, Kremer goes on to say that strong IP protection can lead to wasteful duplication of research into existing, substitute and imitation products.
- 17 Heller and Eisenberg argue that rather than encouraging research, stronger intellectual property rights may lead paradoxically to fewer useful products for improving health. Strong intellectual property protection can lead to a spiral of overlapping patent claims in the hands of different owners, increasing the transaction costs of research downstream. The high transaction costs and complex obstacles to an inventor mean less or slower new research, a common situation with biomedical research.
- 18 Others have argued that this system is outdated, and too inflexible. Fundamental shifts in technology and the economic landscape make it unworkable and ineffective. Designed more than 100 years ago to meet the simpler needs of an industrial era, it is an undifferentiated, one-size-fits-all system. The growing difficulty of restricting imitation, and the rate of increase in new technology, makes the current system difficult to enforce and prone to error.
- 19 However, there is also likely to be an economic case. Economically, the social losses resulting from inefficiently high prices are likely to be much higher for

* This supports the argument that additional public funds are still needed for research and development. Publicly funded research options are discussed in more detail in annex 5.

drugs than for, say, CDs.* Thurow argues that a more differentiated approach is needed, taking account of countries income levels and the importance of the technology for basic human needs.

- 20 In addition, there are arguments, both moral and economic, that even if the intellectual property regime overall is reasonably efficient, it is inappropriate for pharmaceutical products in developing countries. The moral arguments are obvious. Pricing people out of the market for consumer products, so as to produce an incentive for innovation, is different from pricing them out of the market for life-saving drugs.
- 21 Oxfam and VSO have argued that the current balance in TRIPS is causing inexcusable problems of affordability for the poor in developing countries. Oxfam argue that, following successful lobbying on behalf of Western pharmaceutical companies, WTO Member States agreed to the patent life and the terms of the protection in TRIPS being too heavily weighted in favour of the company at the expense of the consumer. Both campaigns have suggested using the existing flexibilities within TRIPS to safeguard developing countries HIV/AIDS and public health concerns.

Section 2: Intellectual property protection: R&D, prices and FDI – the empirical evidence

Research and development

- 22 While there is empirical evidence to support the theory that intellectual property protection is likely to lead to more research and more innovation, little work has been done on the impact on research and development (R&D) specifically for *developing country* diseases. This is obviously the focus of the project. In a recent article, Lanjouw and Cockburn examine the impact of the increase in global intellectual property (IP) protection (as represented by TRIPS Agreement) on R&D in tropical diseases, including malaria.
- 23 Using interviews with pharmaceutical companies, the statistical information available on the number of patents filed and on scientific citations, they gathered empirical evidence on the impact of the strengthening of the global patent system on R&D investment and product development for tropical diseases. They conclude that, while it is possibly too early to tell (TRIPS was only implemented in developed countries in 1995), there has been an increase in the research related to treatment of malaria, but this result does not hold for new research directed towards *other* tropical diseases.
- 24 We can infer that, while IP protection might provide incentives for increased R&D in tropical diseases, the difficulty of the science and/or the lack of a market for treatments remain critical in research decisions. Anecdotal evidence from an Indian pharmaceutical company (CIPLA) suggests that once India has fully TRIPS-compliant patent protection, they will become more of an

* This is because the willingness-to-pay of consumers in developed countries for life-saving drugs is likely to be very high relative to production cost. Hence the profit-maximising monopoly price will be high resulting in large numbers of poor people in these countries being priced out of the market. In technical terms, the demand curve is much steeper and hence the consumer surplus lost as the result of monopoly pricing much greater.

R&D based, rather than generic, pharmaceutical company. However, they will be interested in developed world diseases such as heart diseases and obesity i.e. those where there is a guaranteed and profitable market.

- 25 There have been some attempts to encourage R&D for the less widespread diseases. Orphan Drug legislation in both Europe and the US is an attempt to make the conditions for R&D into these diseases more favourable. Orphan diseases, while not necessarily tropical diseases or developing country diseases, share some characteristics. They are uncommon diseases in these regions, affecting relatively few numbers. The legislation that is put in place offers added incentives for R&D, including fast track approval processes, and in the US tax credits on the funds invested in research.

Prices

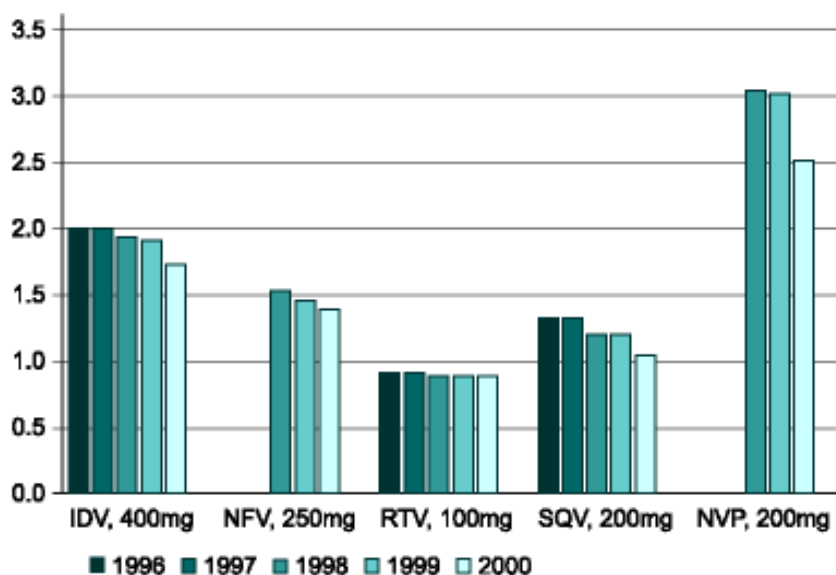
- 26 The empirical evidence available does support the proposition that competition leads to lower prices. Competition can come from another patented product, a re-engineered imitation product, an alternative substitute product, and once off-patent, other generic products. For example, the patented products *Lamivudine* (also known as *3TC*) and *Zidovudine* face competition from generic versions produced in India and Brazil.* Furthermore, customers can substitute branded aspirin for generic aspirin, or other pain relievers such as ibuprofen, paracetamol and even homeopathic products.
- 27 Studies from the US demonstrate that the dramatic rise in generic sales (not imitation) of off-patent products since 1984 has held down average prices for drugs that are no longer protected by patent. They estimate that the increased use of generic drugs reduced the cost of prescriptions to the US Health budget, by between US\$8-10 billion in 1994. Duke University researchers found that within 6 months of entry, the price of the generic was 50-60 per cent of the patented price.
- 28 The International Federation of Pharmaceutical Manufacturers Associations (IFPMA) suggests that there are fewer and fewer (breakthrough) drugs where there is truly no other substitute therapy. While *Tagamet* (1977), an anti-ulcer drug, had no substitute for six years until *Zantac* entered in 1983, *Invirase* (1995), an anti-HIV protease inhibitor, was followed by *Norvir* (1996) after only one year. This indicates that even patented products face competition from substitutes.
- 29 Competition from imitation products from countries not recognising product patents also puts low-price substitutes on the market. There are numerous pricing reports produced to demonstrate the huge differences between generic versions and patented products. For example, a 1999 Médecins Sans Frontières (MSF) pricing study for *flucanazole*, a treatment drug for opportune infections common to HIV patients, asserts that the patented *Diflucan* offered by wholesalers ranged from US\$9.34 per 200 mg capsule in the private sector in South Africa to US\$ 27.60 in Guatemala. While Indian pharmaceutical CIPLA offers a generic version of *flucanazole* at US\$ 1.26 per 150 mg capsule and Thailand Biolab's price is just US\$ 0.60 per 300 mg. The graph below

* Work done by the Treatment Access Forum in April 2000 indicated that the price of *Lamivudine* varied from \$50 for a months dose for the generic version in India through to \$208.80 for the patented producer in Malaysia.

demonstrates the impact on prices of anti-retrovirals from generic competition in Brazil.

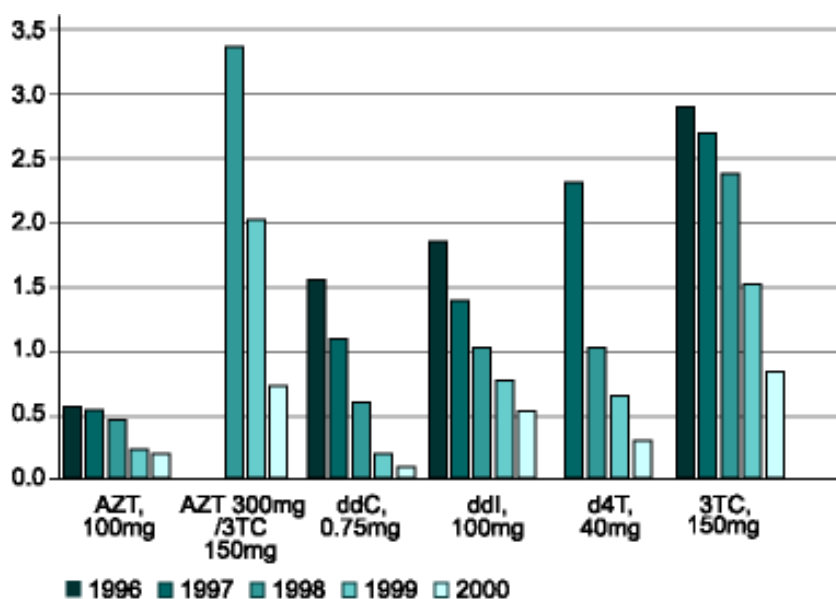
Prices of Brazilian antiretrovirals

Price stability without genetic competition



Prices of Brazilian antiretrovirals

Price reduction from genetic competition



Source: UNAIDS, Brazilian Department of Health. Reproduced in Perez-Casas (2000)

30 One major concern is that, once all countries become fully TRIPS-compliant this source of competition will diminish, reducing the downward pressure on the prices of patented drugs and putting them out of the reach of the poor. However, as we have noted, competition may also come from other patented products, and under strong IP protection this may in fact increase. Watal has estimated the maximum likely increase on prices of implementing TRIPS in India to be between +25% and 250% – with corresponding reductions in social welfare. Price increases are predicted to be highest where there are few

substitutes – and are dependent upon assumptions about how price sensitive demand is.

Trade and Investment

- 31 The intellectual property regime could have a strong impact on international trade in goods and services, Maskus and Penubarti have estimated such effects. Using an econometric model of trade flows, they found that strengthening a country's patent regime would lead to a significantly positive, although small, increase in trade. This effect is particularly strong in large developing countries with a copycat industry, indicating that the total benefits from trade expansion will outweigh the displacement of that local industry. The effect was weaker in small developing countries with low incomes. Econometric work on the relationship between foreign direct investment (FDI) and stronger IP protection is scarce and the conclusions ambiguous. Maskus analyses the work done to date and tentatively concludes that the findings indicate levels of FDI increase with IP protection in developing countries. Correa also studied the foreign investment-intellectual property relationship and found this to be inconclusive due to the multiple factors influencing FDI. Furthermore Gold and Gruben who perform cross-country analyses of growth determinants, find no strong effects of patents on trade growth.
- 32 To conclude, the empirical evidence is scarce. TRIPS has only been in effect for six years and in developed countries only. It cannot yet provide a robust picture of the impact of the intellectual patent regime on new research into developing country diseases, and any possible wider benefits to developing countries in terms of better trade, investment and growth prospects. There is stronger evidence to support the simple assertion that more competition leads to lower prices. We can be reasonably sure that once off patent, there will be greater competition in general. However, that is not to say that there is no competition while under patent, or that once off patent we have a freely competitive market. For developing country diseases where there is a small market, there are fewer suppliers and hence less competition. Intellectual property protection puts in place the right incentives for new research, but this alone is not sufficient. The willingness and ability of customers to pay for new inventions is also necessary. The evidence does demonstrate that prices will fall from the monopoly levels, once off patent. Many poorer consumers are unable to purchase the latest health products if they are patented thus leaving millions in developing countries unable to purchase the latest therapies. Having said this, in cases where there are relatively high set-up costs, the total size of the market needs to be sufficient to encourage multiple suppliers and thus generate competition and price reductions.

Section 3: Patent protection and access to anti-retrovirals – the public debate and the UK government's response

- 33 The previous section discussed the impact of competition on providing low cost alternatives and keeping downward pressure on the price of patented products. This section considers in more detail the costs and benefits to developing countries of using patented *anti-retroviral therapy* (ARVs) to treat HIV sufferers, a subject of much debate. See Section 5 for a discussion of the

intellectual property related policy options aimed at lowering prices of patented products, many of which have been proposed by those lobbying to lower the price of ARVs.

- 34 Last year the South African government and the South African pharmaceutical industry association began a legal battle, which has since been resolved, over the proposed introduction of the South African Medicines Act. The pharmaceutical industry claimed that the Act contained certain provisions that were inconsistent with the TRIPS Agreement and did not protect their rights as patent holders. This Court case fuelled the international debate that patent protection puts essential medicines out of the reach of those that need them. With one in four adults in South Africa estimated to be HIV positive, and patented ARVs typically being sold for \$10,000–\$15,000 per person per annum in the West, this has also raised awareness of the potential impact of patent protection on the HIV/AIDS pandemic. The disease is the primary cause of death in Africa.
- 35 To tackle this pandemic on a global scale there are a number of factors: international political will, helpful economic policies (e.g. competition and tax policy), improvements in health facilities and efficient delivery systems in the affected countries, tackling corruption in the trade in drugs as well as lower costs for drugs, greater efforts at prevention and research into the possibilities of an AIDS vaccine.

Not just the cost of the drugs

- 36 In 1998, using 1994 statistics, WHO and UNAIDS compared estimates of the cost of providing ARV drugs to all those living with HIV in fifteen developing countries. Costs ranged from less than 1 per cent of health expenditure in China, to 81 times the health expenditure in Uganda – more than three times Uganda's national income (as measured by GNP). Prices of the drugs have since fallen, but *total* costs of treating AIDS patients demonstrate the magnitude of the problem we are dealing with.
- 37 Additionally the current state of developing country health care systems is such that, even if ARVs were available, they could *not* be effectively distributed and monitored without major improvements to these systems. Unlike vaccines, HIV requires on-going treatment and therefore a long-term investment in the health budget.
- 38 The costs of treating HIV go well beyond the cost of drugs for opportune infections, and anti retroviral therapy. ARVs especially are complex and potentially toxic to administer. Therefore access to trained medical staff is essential. In order to reduce drug resistance and increase effectiveness a combination of ARV's are used. Combination therapy is not fixed and may change if a particular combination does not work or has an adverse impact on the patient. Furthermore, specific combinations are seldom successful for more than one or two years as the virus builds up a resistance to the diseases. Taking all of these factors into account, in addition to regular medical advice and care, access to a range of drugs is necessary. Even then, some estimates suggest long-term combination therapy may only be effective for 50 per cent to 80 per cent of patients.

- 39 Drug resistance is a major fear of health experts world-wide. HIV is a complex virus that develops resistance to whatever ARVs are used. Taking an inappropriate combination or misusing dosage can increase the opportunities for drug resistance. Because like the disease itself, drug resistance can be passed on during unprotected sex or infected blood, resistance is not only a problem for the individual, but for the community as a whole, and ultimately the whole world.
- 40 The current state of developing country health care systems is such that even if ARVs were available, they could *not* be effectively distributed and monitored without improvements to these systems. Unlike vaccines, HIV requires on-going treatment and therefore a long-term investment in the health budget. Lack of symptoms, reluctance to know one's HIV status due to the stigma attached, the cost of diagnosis, and the lack of any affordable treatment all mean that many people in the developing world do not discover they are HIV positive until many years after they were infected when they contract an opportunistic infection. But more affordable treatment and diagnosis should encourage earlier diagnosis leading wider social benefits from reduced transmission, as more individuals know their status sooner, and receive treatment.
- 41 To conclude, the extent of the public health pandemic across the developing world, and especially in Africa, is such that tackling the diseases should be both a national and a global priority. There are significant benefits to be had from treating HIV sufferers not just in terms of the benefit to the individual, but to the country in terms of having a healthy population to contribute to wider social and – via productivity and employment – economic goals. Improving HIV/AIDS prevention, diagnosis and treatment will reduce rates of transmission, provide an impetus to strengthen the national health care system which will help other non-HIV-positive nationals. However, problems with the toxicity, effectiveness and drug resistance of ARVs are such that sufferers must have access to health care and countries need a long-term strategy that guarantees access to the drugs. Furthermore, a concerted approach needs to be taken to change social behaviour now, to lower the number of new cases, reduce transmission rates and bring the pandemic under control.
- 42 Action is therefore required on a number of fronts: health promotion, access to condoms, health system development and more affordable drugs. A policy option for differential pricing which could be applied to ARVs as part of a global strategy is developed in the next Annex. As the price of ARVs comes down to more cost-effective levels, specific pilots to tackle target (high risk) groups and mother to child transmission should be priorities for this strategy.

Section 4: Other non-patent related impacts on price

- 43 Patent protection is not the only cause of high health product prices. A study by Bala and Sagoo asserts huge variations in the price of *Zantac* in developing countries, despite it being off patent and available from multiple sources. A 150mg capsule in India cost only \$2, but in South Africa it was \$116.
- 44 Competition policy is key: despite not having patent protection, a number of countries without an appropriate competition policy leave the originator's drugs

to be marketed exclusively, even with cheaper generic drugs available on the world market which they could import. This artificially depresses the potential supply. As a result, the prices of some drugs in the developing countries of Africa and Latin America are higher than in more affluent developed countries.

Table 4.1 Retail prices of 100 units of the anti-ulcer drug Zantac (ranitidine) 150mg (\$US)

India:	2
Nepal:	2
Pakistan:	21
Korea:	61
Zambia:	82
Bolivia:	94
Senegal:	100
Burkina Faso:	105
South Africa:	116

- 45 Other factors influencing national prices include: tariffs and taxes, price controls, government price negotiations and mark-ups, negotiating power of the purchaser, procurement policy – including competitive tendering, bulk purchase opportunities and exchange rates. There is much greater scope to negotiate good prices, including for patented products, when there is a bulk order, guaranteed and continuous demand e.g. as is largely the case for UNICEF and the purchase of child immunisations. There is a role for the bilateral and multilateral assistance programmes to provide advice on *all* of these factors and making (safe) generic versions available, as part of support to the health sector.

Section 5: Policy options and recommendations

- 46 In this section we examine alternatives and changes to the current system of intellectual property protection designed to encourage both increased research and development into developing country diseases and ensure that they are made available to the poorest at affordable prices. Obviously, there are additional policies that are currently being pursued in parallel, such as direct public funding of research into new developing country diseases. For example, the UK's Department for International Development (DFID) and Medical Research Council (MRC) have both funded programmes of malaria research. (These policies are considered in the annex on policy measures to strengthen the incentives for research and development). Addressing the issue of the size of the potential market for developing country diseases as an incentive for new R&D is addressed in the annex on the global fund for health. Furthermore, specific issues relating to differential pricing are considered separately in the differential pricing, parallel trade and access to health products annex.

Intellectual property buyouts

- 47 Once knowledge is created it is socially optimal for it to be available for everyone to use for free as the additional cost for any extra customer is zero. As we discussed in section 1, the patent system is sub-optimal in that it allows prices to be charged above manufacturing costs, which has the effect of excluding poorer people. One policy option would be to purchase the patent or

intellectual property, providing adequate compensation to the inventor for the research, and thus putting the information in the public domain, so that production would be competitive and prices would be driven down to marginal cost. *

- 48 This option is similar to the advance purchase commitment in that it demonstrates a clear commitment to purchase the invention – supplementing the willingness to pay by the customer, and enhancing the incentives to the inventor or researcher. The key difference is with the patent buy-out, the Government or international community pays up front for the research, and can then either put the information in the public domain for competitive production or auction the patent to any bidder. This auction could be a competition for the right to the patent and/or for the lowest price at which they will agree to sell the product on the market.
- 49 The key issue is determining what is the right price to pay for the patent in the first place. Economically, the efficient price would be one that reflects the net social benefit resulting from the patent since this would produce the correct incentive for firms to invest in research. However, estimating this benefit is extremely difficult.* Alternative options would look to the market to make such estimates; for example, the value of the patent could be determined by an auction among manufacturers, (i.e. generic and R&D based pharmaceutical companies in the case of drugs).⁺ This runs into problems of collusion among the players and providing the right incentives for firms to put in honest bids, if they know the government is going to buy the patent out. Furthermore, in the case of vaccines, with such high start-up costs and specialised knowledge required, there are currently only a handful of pharmaceutical firms that are potential alternative producers. For a more academic treatment of the issues see Kremer, 1998.
- 50 The reality is not as simple as one patent per product, and each product is the output of a number of patented inputs – it is therefore not necessarily the case that a single patent would be purchased, but rather one or more patents, in a range of countries. Also, the government needs to decide when it is worth exercising this option. For example, how does the government determine whether it is this invention or the yet to be seen outcome of other research, that it should buy? An estimate, say provided by a combination of experts, about the size of the social value above the private value and how long before a superior substitute arrives, would be necessary.
- 51 We recommend that the advance purchase commitment discussed in the global fund for health annex does not rule out the **option** of using the Fund to purchase a patent. The difficulties of valuation and the potential for use of auction would require further detailed consideration

* This option is similar to offering a prize for a specific invention, and has been used with success in the past in the United Kingdom. For example, over 200 years ago a prize was offered by the British government for an invention that would allow ships to accurately determine their longitude, resulting in the invention of the first accurate chronometer.

* Although not necessarily any more difficult than making similar estimates in other sectors, such as transport and education, where it is necessary for governments to calculate the optimal subsidy.

⁺ This could also include a mark-up designed to cover the additional social value, which provide even more incentive for the R&D to take place.

Compulsory Licensing

- 52 Within the TRIPS agreement there are various Articles which relate to exceptions to the general system of Intellectual Property protection. Similar to the patent buy-out option, under restricted conditions, Article 31 of the TRIPS Agreement allows compulsory licensing and government use of a patent without the authorisation of its owner. This can only be done under a number of restrictive conditions aimed at protecting the legitimate interests of the right holder. The authority applying for a licence must have first attempted, unsuccessfully, to obtain a voluntary licence from the patent holder on reasonable commercial terms. Even under compulsory licensing adequate remuneration must be paid. The authorisation that is granted under compulsory licensing must also meet certain requirements. In particular, it cannot be exclusive, and as a general rule is granted predominantly to supply the domestic market. The failed negotiation clause can however be waived in the case of national emergency, extreme urgency or for non-commercial public use. Although this is not specified further, many have interpreted this as to allow for issues of national public health.
- 53 Compulsory licensing can also be authorised under conditions that constitute an abuse of intellectual property rights having an adverse effect on competition in the relevant market.* Such abuse has to be determined to be anti-competitive after due judicial or administrative process. The most common ground under national patent laws permitting compulsory licensing is “non-working” i.e. when a rights holder is not supplying the patented product in the patent granting nation.
- 54 WTO member governments therefore face various policy options so as to operate the system of intellectual property using the various articles specified in the TRIPS agreement that already allow exceptions to general treatment. However, without greater common international understanding on the interpretation of these flexibilities, and on examples of what constitutes “national emergency”, for example, adult HIV prevalence greater than fifty percent, “extreme urgency” etc., this could lead to recourse to WTO dispute panels.
- 55 The use of compulsory licensing is also specified in the TRIPS agreement to be predominantly for the home market. The implications for the majority of developing countries without their own pharmaceutical industry are unclear, as is the option of licensing a non-national firm to produce for the domestic market.
- 56 Broad-based use of compulsory licensing provisions is likely to undermine the incentive for R&D and lead to downstream problems in ensuring that the right incentives are in place for the additional research into drugs and vaccines necessary for tackling the disease burden of developing countries.
- 57 While WTO dispute resolution panels will ultimately determine and hence define more precisely the interpretation of flexibilities under TRIPS. More should be done to come to a common understanding on the conditions that warrant use of the flexibilities, especially compulsory licensing. We support the

* TRIPS Article 40

proposal that, as a first step towards this, the WTO TRIPS Council should seek to clarify the existing flexibilities with the TRIPS Agreement at the earliest, as one way of helping WTO members achieve the health targets set out at Okinawa.

Public Private Partnerships

58 Relatively new combinations of public funds and private know-how initiatives (so called public-private partnerships) have been established to increase research in developing country diseases. International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Venture (MMV) and the Global Alliance for TB (GATB) are three such initiatives designed to produce an HIV/AIDS vaccine and new drugs for malaria and tuberculosis respectively. If these result in new drugs and vaccines for market, the intellectual property is already subject to contractual arrangements between the initiative and the private firms involved, as a condition of accessing public funds for research.

59 Let us consider the case of IAVI in more detail. IAVI's mission is to accelerate the development, manufacture and distribution of HIV/AIDS vaccines at accessible prices to the public sector of developing countries. The intellectual property terms in its research agreements reflect this mission and have two major objectives:

- To assure that IAVI has freedom of action to use the results of the research it has funded; and
- To provide additional intellectual property protection to collaborators, to increase the incentive for investment in development and production of HIV vaccines.

A third minor objective is to return funds to IAVI for furthering its mission, through small royalties on IAVI-funded patents for sales in the developed world.

60 While it is anticipated that the private firm involved in research and development of a vaccine will also be involved in its ultimate manufacture, in the event that the firm is unable to deliver the vaccine at "accessible prices" to the public sector of developing countries, IAVI has the freedom to seek alternative suppliers. Carefully crafted contractual agreements are therefore entered into with industrial partners in order that IAVI can achieve its objectives and limit the risks to, and protecting the rights of, the private company as much as possible.

61 Intellectual property issues are crucial in these contractual arrangements, and like TRIPS or any national system itself, a balance must be struck between the appropriate incentive for investment in R&D and the price paid by the end consumer. Depending on the balance of funds and risk between the public and private partners, the need to ensure the right incentives for private sector to invest are weakened. Under such public-private partnership arrangements, the use of public funds should be used to ensure patent arrangements that mean prices to the end consumer are affordable.

62 To conclude the issue of access to patented products for developing country diseases needs a balanced approach. On the one hand, we want to maintain the right incentives for additional research and development into these

diseases, and on the other hand to ensure that the prices are affordable as far as possible. The options recommended here are to explore further the flexibilities with respect to the use of compulsory licensing within TRIPS, and to work toward an international agreement on the use of these flexibilities so as to contribute to meeting the Okinawa infectious diseases targets and the international development health targets more generally.

- 63 In order to strengthen the incentives for R&D into these diseases, protection of minimum standards of intellectual property need to be maintained and broad based use of compulsory licensing is not recommended. This is however not sufficient. We recognise that additional policies are necessary to put in place the purchasing power of the market. This is recommended in the form of an advance commitment to purchase new, more effective products. Finally, as returns are still likely to be higher on Western health products where people have a higher willingness and ability to pay, we recognise there is a role for publicly funding additional research into these diseases. Where this is the case, public funds should be used as leverage for more attractive patent arrangements that ensure affordable prices to the poor.

Annex 4: Differential pricing, parallel trade and access to health products

Introduction

1 This annex considers the possible role of tiered pricing and parallel trade in increasing access of the poor to health products. It complements, and should be read in conjunction with, annex 3 on the impact of intellectual property rights. In the majority of cases the necessary products are not patent-protected. Of the 300 drugs currently on the WHO Model List of Essential Drugs, less than 5 per cent are estimated to be under patent protection anywhere in the world.¹ But the context of the growing public interest in the impact of intellectual property protection on the price of these medicines and treatments in the developing world focuses on the minority which are still under patent. And in particular the drugs needed to fight the relatively new disease of HIV/AIDS that are inevitably on patent. We discuss policy options such as tiered pricing and parallel trade since they have the potential to reduce the prices that developing countries face for patented medicines.

2 In Section 1 this annex explores the economic theory behind tiered pricing and the market conditions associated with it. The current situation in the global pharmaceutical industry is examined in Section 2, and how this relates to the theory. In section 3 we consider the policy options open to the international community to increase access to drugs, and make recommendations for the international community to consider further.

Section 1: The theory – Price discriminating monopolists, Ramsey pricing and parallel trade

3 In April 2001, the World Trade Organisation and the World Health Organisation hosted a workshop on “Differential Pricing and Financing of Essential Drugs” in Norway. They adopted the term differential pricing to mean the adaptation, in some measure, of prices to the purchasing power of consumers in different countries. In this paper for ease of comparison we adopt this same definition for both the terms “tiered pricing” and “differential pricing”, terms which are used synonymously in the wider international debate. In the context of pharmaceuticals, differential or tiered pricing is therefore charging different prices to different countries for the same medicine in response to the different price sensitivity of demand in these countries.

Price discriminating monopoly

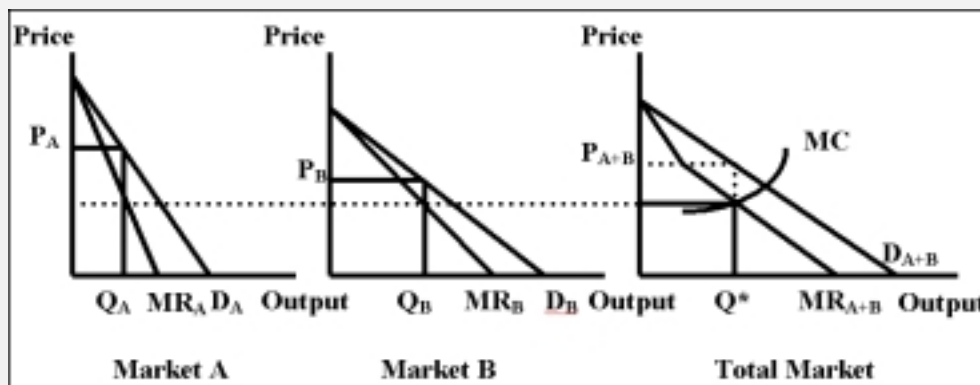
4 It is helpful to take time to understand the theory underlying the current discussion of tiered pricing and parallel trade as policy options. Let us first examine the economic concept of a price discriminating monopolist. In the theoretical case, there are a number of assumptions necessary for firms to be able to practise price discrimination:

¹ Watal 2001

- there is some degree of monopoly power of the supplier;
- the total market can be divided into markets for different ‘types’ of consumer;
- in each of these markets there are different demand curves and sensitivities to changes in price;
- a single price is charged in each market; and
- it is not possible to resell the product between markets. The markets are separated either on the basis of time or geographically.

Box 1: For the economic enthusiast – the diagram

The combination of these assumptions can be represented diagrammatically as follows:



This theoretical situation is referred to by economists as “third degree price discrimination”. In the example demonstrated above the market is divided into two segments, for simplicity we can call them, A and B. The total market output (q^*) is determined at the point at which the cost of producing the last product (incremental or marginal cost) is equal to the price it can be sold at. In other words when marginal cost is equal to marginal revenue. This output can be split between the two markets A and B, depending on the point at which the marginal cost covers the marginal revenue to be made in each market. This results in the firm deciding to sell q_A for market A and sold at p_A and q_B for market B for a price of p_B . The firm makes a profit in both markets of $abcd$ and $efgh$.

Note that the assumptions also assume that the marginal cost of production is the same for both markets and A and B.

These assumptions, and how they relate to the pharmaceutical industry are examined in more detail in Section 2.

Ramsey Pricing

- 5 An industry that is largely based on generating new ideas and innovations can be referred to as research-based, and generally spends a higher percentage of sales on research and development (R&D) than most other industries. For example in the United States, research-based⁺ pharmaceutical companies spent 21% of sales revenue on R&D, compared with 4% for US industry

⁺ “Research-based” is a term used to distinguish these companies from generic or imitation pharmaceutical producers.

overall.⁺ This R&D investment is sometimes referred to as global joint costs. All countries have the opportunity to benefit from the investment in R&D, and consequent new products. But the R&D costs are not necessarily borne by all consumers if the firm charges different prices in different markets – as demonstrated in the diagram above. If the firm is to stay in the business, it needs to ensure that *in aggregate the total costs* are covered.

- 6 Further to the theory of the price discriminating monopolist, the theory of Ramsey pricing demonstrates how under certain market conditions it is socially optimal for firms to charge different prices to different users and cover the full costs of the product in aggregate. The different prices charged are dependent upon how sensitive the type of consumer is to changes in the price. In the example given above, consumers in market A are relatively price insensitive. As price increases, there is a relatively small drop in total quantity demanded. In market B, with a flatter demand curve, consumers are relatively price sensitive – a price increase has a relatively large fall in total demand.
- 7 The theory implies that the socially optimal result is one where consumers are charged different prices reflecting their willingness to pay and total profits to the firm are sufficient to cover the R&D costs.
- 8 The problem of pricing to cover joint costs is exacerbated by the fact that these costs are largely sunk at the time of product launch, and in a competitive industry prices will be driven down to incremental costs. The use of intellectual property protection as a response to assist research-based firms make an adequate return on the investment, by allowing the firm exclusive rights to market the product for a fixed term, is discussed in more detail in the impact of intellectual property rights on access to health products annex.

Parallel trade and international trade

- 9 What happens if the firm charges the uniform price (shown by p^* in the diagram)? Under these conditions the producer sells up to the point where it can sell anywhere in the world and cover marginal costs. This would be the result if the markets were no longer separated, and the products were freely traded across the two markets. This is often referred to as parallel trade.
- 10 Under these conditions does the theory predict that consumers and producers will be better or worse off? Economic theory suggests that if the firm has market power and the other assumptions related to price discrimination listed above apply, the firm maximises profits by differentiating prices. However, under more competitive circumstances this will not be the case.
- 11 In the case of the price discriminating monopolist, an increase in parallel trade and a shift to uniform prices will have an impact on both price-sensitive and price-insensitive consumers. This will be dependent both upon the price sensitivity of each consumer is, and the overall difference between the differential prices charged at each “tier” and the uniform price. The uniform price in this theoretical example demonstrates an increase in price for both the price sensitive and insensitive markets – thus making these consumers worse off. The theory of Ramsey pricing suggests that in aggregate the net effect is to make both consumers and producers as a whole, *worse off under uniform*

⁺ Danzon, 2000

pricing. We examine the significance of this further in Section 3 on policy options, and how the situation might be adapted so that all groups gain from tiered pricing. ⁺

Section 2: Do the conditions fit the global pharmaceutical industry? - the evidence

- 12 In the paper prepared for the WTO-WHO Workshop, Watal asks “if, as economic theory suggests, tiered pricing can be a win-win situation which is good, or at least not harmful, to consumers and beneficial to producers, why is it not more commonly practised?” Price discrimination is a situation that we find in a number of industries. In the rail industry for example, rail operators charge different prices for different types of customers, peak, off-peak, youths etc. and in the provision of utilities such as gas and electricity. Does this also apply to the pharmaceutical industry?
- 13 If we refer back to the assumptions necessary for price discrimination listed above, we see that a number of these do apply to the pharmaceutical industry, and that we need to distinguish between the research and development (R&D) based pharmaceutical industry and the generic producers.

Market power/monopoly supplier

- 14 The R&D based pharmaceutical industry faces high fixed costs – similar to the rail industry or utilities. The total sums invested in R&D are estimated to be on average \$400-\$600 million ^{*} to bring one successful pharmaceutical product to market. High fixed costs act as a barrier to entry, and as a force for mergers (as bigger firms can benefit from economies of scale and combined facilities). The R&D based industry is therefore dominated by a handful of firms.
- 15 Furthermore, once a firm registers the patent for a new product, it has the exclusive right to market the product. Thus an R&D-based firm exercises market power due to the small number of total firms in the industry, and for specific products becomes the monopoly supplier. That is not to say that once under patent the firm does not face any competition, but competition is limited. In summary, firms in the R&D based pharmaceutical industry do have a degree of market power.
- 16 There are fewer arguments for these conditions applying to the global generic pharmaceutical industry (used here to refer to producers of off-patent products, rather than firms producing imitations of patented products.) As the industry invests far less in R&D, the costs of entry are not as high and therefore represent less of a barrier to entry. The generic industry is therefore far more competitive and contestable than the R&D based industry. In other words it is much easier to enter and exit this market. Furthermore by definition, the generic industry produces products which are off-patent and therefore substitutes are available. Where the market is so small that only one producer

⁺ For further examination of the theoretical arguments of Ramsey pricing, the net gain in social welfare from keeping markets separate and charging different prices, and how they relate to the pharmaceutical industry see Patricia Danzon’s “*The Economics of Parallel Trade*”

^{*} Kettler H (2000) p.34

is supplying the market – once this producer is making excessive profits, a rival firm will be free to enter and compete.

- 17 The terms of the transition period for signatories of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement are such that a number of developing countries who are not yet required to fully comply with the TRIPS agreement and have the capacity for pharmaceutical production e.g. India, Brazil, are able to produce imitation products through reverse engineering i.e. analysing a patented product to produce an exact copy. These products provide an element of competition for patented products, particularly in their home markets. However as all countries increasingly put in place the minimum standards of intellectual property protection these industries is likely to develop into R&D based- and/or generic pharmaceutical producers.

The market can be divided

- 18 There are two common divisions of the global market for medicines and health care products. The first division refers to developed and developing country markets – the difference between relatively rich and relatively poor consumers. The second, is the difference between public and private consumers – in other words, those that are covered by a national or social insurance scheme to help cover the costs of health care, and those that bear the full costs of the medicines. Thus one simplification would be to say that the market can be divided in four as follows:

Developed country Public purchaser	Developed country private purchaser
Developing country Public purchaser	Developing country private purchaser

- 19 This is obviously a simplification. There are other consumers such as global procurement by large international development agencies such as UNICEF and local non-governmental, and religious-based organisations who provide health care and advice. But for these purposes one can include large global development agencies within the definition of public purchaser. Similarly small-scale local non governmental and civil society organisations can be included in the definition of developing country private purchasers.
- 20 In reality, the groups proposed above are not homogenous and contain a vast spectrum of income levels and tastes. In particular, in the developing country group – we have both least developed countries (LDCs),⁺ low- and lower middle-income countries^{*}. It will be important to draw a distinction between the

⁺ An LDC is defined as a country scoring below 0.5 on the UN Human Development Index

^{*} A Low Income Country is defined as having a GDP per capita below \$755. A Lower Middle-Income Country is defined as having a GDP per capita between \$756-\$2,995 (World Bank 1999)

poorest countries in the world and those upper middle-income countries with per capita incomes in excess of \$2,996.

In each of these markets there are different demand curves and sensitivities to changes in price

- 21 There is little empirical evidence on the demand function or willingness to pay for pharmaceutical products in developing countries, and/or comparisons of these with developed countries. Having said this, it is possible to draw the assumption that the demand curves are very different between these groups. This is as a result of the average income available for medicines and drugs being very different between each groups.

Developed/developing division

- 22 While this may be true at some aggregate level, within the division, the different burden of disease is very different. In fact the market may be divided again by incidence. Notably there are large variations in the incidence of HIV/AIDS, tuberculosis and malaria geographically, both between different regions of the world and within countries. Furthermore, the strain of the diseases also varies and the same products are not necessarily effective in all regions. There are many different clades of HIV/AIDS and, while the treatments currently available appear to be effective for all clades, it is highly unlikely that a vaccine could be developed that would be suitable for all. Typically in the West the market for products to treat malaria is determined by the size of the traveller's market, whose requirements are for short term highly effective so as to prevent catching malaria, as opposed to treatment and the need for this to be effective in the long run. The BCG vaccine used to immunise against tuberculosis is very effective and widely used in the West, but virtually ineffective in India for example. Thus the demand curves may be very different and in this case for non-price related reasons. In some cases so much so that the demand for a particular drug or vaccine is zero in one of the groups!
- 23 If we take the simple division between developed and developing countries, and further divide the middle income countries and the least developed countries, and the high prevalence countries from the low prevalence countries – we can be reasonably sure that there would be very different demand curves in each of these sub-groups.

Rich/poor division

- 24 Within all countries there is a range of incomes or livelihoods determined by total per capita income, inequality, and levels of self sufficiency for subsistence families. Although there is relatively little empirical evidence on the price sensitivity of demand for pharmaceuticals, particularly among the poor, in general individuals and families with a much lower annual income and greater pressure on that income from other basic needs to survive, will be much more price-sensitive (a flatter demand curve). The developing country middle-class and developed country poor, will be relatively more price insensitive – with a steeper demand curve, but not as price insensitive as the middle class and wealthier consumers in developed countries (an even steeper demand curve).

- 25 Aggregate demand curves are also likely to be lower for the poor rather than the rich. In other words the price at which demand falls to zero, is much lower than for the high income group. (i.e. the demand curve for the poor will intercept the y or price axis much lower than for the middle class, and similarly at the more macro level will be lower for the developing country group than for the developed country group.

Public/private division

- 26 The split between public and private health care consumers is a relatively easy one in the developed countries, where the majority have some national insurance or social insurance that ensures that there is universal access to a minimum standard of health care regardless of income. Those who can afford to and have a higher premium on access to health care can also go to private providers. This group has a higher demand curve in aggregate. Accessing public health care, often means that the purchase of health products is not done by the patient but by a medical professional. As the costs are not borne directly by the consumer, the aggregate market is relatively price-insensitive.

A single price is charged in each market

- 27 Evidence demonstrates that the assumption that a single price for a pharmaceutical product when sold in each market is not readily applicable to the current situation. It is difficult to make meaningful comparisons. The price of the end-product reflects very different national policies on taxes and subsidies, competition in the industry and government procurement practices, transport costs and mark-ups. (The impact of intellectual property rights on access to health products annex demonstrates there are indeed wide variations in the price of drugs across countries and within countries.)

Box 2: The reasons for price differentials

The International Federation of Pharmaceutical Manufacturers Associations list the following reasons for price differentials:⁺

- Government policies such as differences in health care conditions and medical practices, differences in national health care funding systems, differences in reimbursement systems, as well as market- and trade- distorting government interventions;
- Inflation differences and exchange rate changes;
- Variations in per-capita national income and tastes;
- Marketing and sales strategies of patent-holders and distribution chain margins;
- Discounting or donation products to the least developed countries;
- Differences in regulatory systems, product liability laws and tax levels; and
- Differences in the remaining term of patent protection among countries.

⁺ IFPMA, 2000

It is not possible to resell the product between the two markets and the markets are separated on the basis of time or geographically

- 28 If the markets cannot be separated and there is open trade between the two, the low-price sensitive consumers will be able to on-sell the lower price product at a margin to the high-price sensitive consumers. This is often referred to as parallel trade.

The trend is breaking down market separation

- 29 The trend is increasing volumes of global trade, with more countries becoming members of the World Trade Organisation, committed to bringing down national barriers to trade, and trading with one another on the basis of equal treatment. Increasingly the world is becoming a single global market, rather than many separated markets. The economic theory predicts, and empirical evidence shows global economic benefits from increased international trade. The rise in trade has been facilitated by a number of social, political and technological developments; such as the decline in global conflict and the cold war; the world-wide web and the ease of purchasing from abroad; and the increase in regional political and economic agreements (often including free trade) e.g. the single European market, and the North American Free Trade Agreement. The UK White Paper *Making Globalisation work for the Poor* examines the potential impact more generally on development, and how we can maximise these economic benefits for development and poverty reduction.⁺
- 30 The theory of economic international trade benefits and tiered pricing are not inconsistent. Tiered pricing and market separation is beneficial under certain conditions. Under normal competitive market conditions, trade between areas provides greater choice to consumers and puts competitive pressure on firms to increase efficiency and downward pressure on prices.
- 31 As we have noted, the generic or non-patent pharmaceutical industry is a far more competitive industry. The more competitive the industry and the further away from the assumptions underlying the benefits from tiered pricing – the less likely that market separation will be socially or economically optimal.
- 32 Global trading conditions are not differentiated on the basis of whether a product is on- or off-patent. There are currently no specific additional barriers to trade for patented-pharmaceutical products. This implies that markets are not separate for the R&D-based pharmaceutical industry and the patent-protected ones.
- 33 For pharmaceutical products the trend is toward increased trade. Developed and developing country markets are often ‘separated’ to a certain extent by differences in standards. While adapting different standards to different markets may make sense for products such as T-shirts, this is highly controversial when dealing with medicines. While economically it might make sense for cheaper, less high quality products to be produced for more price-sensitive markets, morally when we are talking specifically about life-saving drugs this cannot be advocated unreservedly.

⁺ DFID (2000)

- 34 Markets for patented-pharmaceutical products are separated by where a patent is registered. In other words if a patent is registered in a particular country the patent holder has the legitimate right to market that product exclusively in that country. The rights of patent holders and minimum standards of intellectual property protection for WTO members is covered in the Trade Related Aspects of Intellectual Property (TRIPS) Agreement. The TRIPS agreement does not prevent governments from allowing the importation of goods from the cheapest legitimate international sources. In other words it does not restrict parallel trade.

Section 3: Policy options and recommendations

Introduction

- 35 In Section 1 we summarised the theoretical case for tiered pricing to improve global efficiency and equity and examined the relatively scarce evidence of how this theoretical example differs from the current situation in the pharmaceutical industry. In short, the generic, non-R&D based pharmaceutical industry has more competitive market characteristics, with firms in the R&D based industry more oligopolistic. For patented pharmaceuticals there is often a single supplier (monopoly) of that particular product – although competition can be exerted from substitute and imitation products.
- 36 In this Section we investigate policy options that would assist access to patented products for the poor, by lowering the prices of patented products to them – without causing an adverse impact on other consumers, and still ensuring that producers are still able to make an adequate return. The options we present here are at initial stages only. We recognise they may be difficult policies to implement and require international action – rather than the action of any one country. With little empirical research to draw upon, they also require more detailed investigation of their potential impact and of the precise practicalities of implementation.

More research

- 37 With this lack of empirical analysis, more work is needed to understand the potential impact of parallel trade and tiered pricing on access to health products for the poor; and to identify how alternative forms of tiered pricing might benefit the poorest. In particular there is little evidence into whether the industry and market characteristics with respect to certain products and certain regions in the world are similar to the theoretical assumptions that would imply tiered pricing is socially optimal.

Facilitative framework for tiered pricing

- 38 As demonstrated above, there are a number of characteristics of the R&D - based pharmaceutical industry and its patented products that are consistent with the underlying theoretical assumptions. These point to tiered pricing as a preferable pricing strategy to uniform pricing, both from the point of view of consumers as a whole and producers themselves. One option, given there is some relation between the theoretical assumptions and the current situation for patented products, is to facilitate market separation – the key assumption

necessary for tiered pricing. At the WTO/WHO workshop on tiered pricing, Adrian Otten of the WTO's Intellectual Property Division, concluded: "there was broad recognition that tiered pricing could play an important role in ensuring access to existing drugs at affordable prices, particularly in the poorest countries, while the patent system would be allowed to continue to play its role in providing incentives for research and development into new drugs."

- 39 With the trend to increased trade, and bringing down barriers – this necessary market separation will not be easy to achieve. More research and analysis are needed into the possible modalities and impacts in particular to ensure that pharmaceuticals designed for the poorest do not leak back into higher priced markets undermining the desired wider social benefits. Section 2 demonstrated how difficult it is to divide the market along the lines of different demand characteristics. With the trend to increased trade and bringing down barriers, limiting trade in patented pharmaceuticals may not be easy. There are obviously various ways of separating markets, and optimal separation (i.e. where the markets are largely based on similar price sensitivities) will not necessarily be the divide that allows for a simple geographical separation.
- 40 The question of the impact of tiered pricing and restricting parallel trade on the more price-insensitive or Western consumers of health products has been raised. However, what is being proposed here, is not to increase the price of patented medicines in developed countries, but to maintain prices in the Western markets while and in addition producing benefits for the poorest countries, by selling to them at a differentiated lower price. But this price needs to cover at least the incremental costs of production, and ensure that the total revenue on global sales to the firm ensures that adequate returns are made on the costs of R&D as well as production.
- 41 In the first instance, we recommend that more thought be given to the idea of differential treatment for developed, middle-income and the least developed country markets, and research undertaken into the likely impact of differential prices in each of these markets. Furthermore, we support the work of the European Commission's who have also been examining the possibilities for tiered pricing and parallel trade in their *Programme of Action: Accelerated action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction*.⁺ At this stage we do not propose using the TRIPS agreement to affect policies on tiered pricing or parallel trade which it already allows.

Prices and non-patented products

- 42 As we have noted in the reasons for price differentials box, different prices can be charged in different markets for a variety of reasons and in practice already are in some markets. At a broad level we support fully policies at both the national and international level that improve market efficiency and consequently lower prices. This includes the range of policies covered elsewhere in the PIU study to lower the cost of medicines to the poorest, such as a Global Fund for Health – which could directly subsidise the cost of essential medicines, and other cost-effective health products for the poorest. Furthermore, we should support developing countries procurement and

⁺ EC (2001)

competition policies, so that as far as possible, they can maximise the potential benefit from competition from more than one supplier, negotiated price discounts, bulk purchasing etc.

Annex 5: Policy measures to strengthen incentives for research and development

- 1 Policy measures to strengthen incentives for research and development of new, more effective products can be broadly classified into three groups: “push”, “pull”, and regulatory measures:
 - “Push” measures aim to stimulate research and development activity from an early stage in the product development timeline, for example through additional or better targeted R&D funding;
 - “Pull” measures aim to strengthen incentives for research and development by improving the prospective value of the market for producers of effective new health products, for example through a credible commitment to purchase effective new products as they become available in the future; and
 - Regulatory measures aim to speed up the international approval and licensing of effective new products, so that they might be made available more quickly to those that need them.

Eligible diseases and products

- 2 **Recommendation:** To maintain an appropriate focus for additional public support for R&D, **additional funds should, in the first instance, be restricted to activities related to new products to tackle HIV/AIDS, TB and malaria.** This restriction should be subject to periodic review, with a view to later inclusion of research on products to tackle other diseases whose burden falls predominantly on the world’s poorest people. It should be noted that the capability and capacity for research into these diseases is limited, and consideration should be given to developing the necessary capacity as part of additional public support. **Recommendation: products eligible for support should include vaccines, diagnostics, drug treatments, other – as yet unknown – products, and significant improvements to the efficacy of existing products.**

Targeted support for research and development

- 3 The existing range of products to tackle HIV/AIDS, TB and malaria are neither effective enough, nor sufficiently robust to new strains of the diseases, to offer a rapid, sustainable solution to preventing, diagnosing and treating these diseases. Vaccines to immunise against HIV/AIDS and TB do not yet exist, and no long-lasting vaccine to immunise against malaria is available.
- 4 Widespread use of condoms can help prevent the spread of HIV/AIDS, but socio-cultural and economic barriers to their use prevent universal uptake. Bednets impregnated with insecticide to repel mosquitoes can reduce the spread of malaria, but have a limited lifespan and need re-impregnating at regular intervals. Resistance to multi-drug therapy for TB is increasing, as patients find it difficult to adhere to lengthy courses of drug therapy in poor delivery environments. And the incidence of malaria is rising with the rapid spread of *Plasmodium falciparum* strains resistant to existing anti-malarial drugs.

- 5 Despite the absence or decreasing efficacy of existing products, only around 10 per cent of global pharmaceutical R&D activity is targeted at the so-called “diseases of poverty”. This lack of action reflects the difficulties of research, the uncertain chances of success and the long timescale for developing effective new products. It is also due to the absence of effective markets in developing countries for products that emerge from the R&D process. Even where markets do exist, economists have estimated that the social returns to R&D are usually twice the returns to private developers. ⁺
- 6 Targeted public support for research complements policy options to improve the affordability of existing health products and strengthen incentives for private sector research and development. **Recommendation: carefully targeted public support for basic and applied research, including innovative public-private partnerships to leverage private funds and expertise; the creation of a clinical trials platform; and harmonisation of regulations to speed up approval and licensing of new, more effective products.** Each of these components of support is outlined below.

Support for basic and applied research

- 7 Analysis by disease of available information on new products in the development “pipeline” indicates that although there are a handful of products in development to tackle HIV/AIDS and malaria, there is little activity on products for TB. One likely reason for the activity on HIV/AIDS and malaria is that products for both diseases have developed country markets, albeit with different product requirements that make them unsuitable for use in developing countries. In the case of HIV, they are designed to tackle different clades than that prevalent in developing countries. For malaria, developed country markets require products to protect only short-term visitors to malarial regions, not permanent residents. The lack of activity on products to tackle TB is also linked to developed countries’ research priorities, which were re-prioritised in the 1950s and 1960s when TB was all but eradicated using penicillin and other antibiotics. For products to tackle HIV/AIDS and malaria in developed and developing countries, scientific challenges remain but are believed to be surmountable in the medium-term. For TB, the lack of activity on new products means that the scientific challenges are uncertain.
- 8 There is a case for public support for basic and applied research on products to tackle the clades of HIV and strains of TB and malaria prevalent in developing countries. Support should be carefully targeted by disease to ensure that publicly-funded research does not crowd out private research. Instead, public funds should be used where possible to leverage additional private funds through innovative public-private partnerships. An alternative approach is for the public sector to fund and/or undertake basic research, handing emerging candidates over to the private sector for development. This approach was behind many of the existing anti-retroviral drugs used to treat HIV/AIDS.

⁺ Nadiri (1993); and Mansfield et al (1977) in Kremer (2001).

Using existing mechanisms

- 9 Where possible, developed countries should aim to channel additional funds for appropriate research through existing mechanisms, to avoid creating new layers of bureaucracy. In some instances it might be necessary to extend existing eligibility criteria for national research funds to enable access by all institutions and researchers submitting verifiably appropriate and credible applications, regardless of global location.

Public-private research partnerships

- 10 Although there are precedents of ground-breaking products resulting from public research, including the Sabin and Salk vaccines against polio, public research alone is less likely than public-private partnerships to yield timely and effective new products to tackle HIV/AIDS, TB and malaria in developing countries. Public research is usually undertaken at universities and publicly-funded research institutes, and faces a number of challenges additional to those faced by private industry. Publicly owned organisations must compete with private firms for a limited pool of quality scientists and researchers; they must have sufficient political independence to pursue research that meets scientific excellence and cost-effectiveness criteria; and they must be able to stop unproductive work.⁺ Additionally, public research typically attracts far less funding than comparable private sector research.
- 11 Recently, the shared desire of governments, non-governmental agencies, private companies and private foundations to combat infectious diseases has led to a proliferation of innovative public-private partnerships. These match expertise and funds in the public sector with those of the private sector. Substantial “new money” has been made available to researchers, including that from new philanthropists such as the Bill and Melinda Gates Foundation. The arrangements created to facilitate these new partnerships fall into two broad groups: “public sector programmes with private sector participation, operating under the auspices of intergovernmental agencies; and not-for-profit public-private partnerships operating under the national laws of various countries.”^{*}
- 12 Examples of public-private partnerships to research and develop new products to tackle HIV/AIDS, TB and malaria include the International AIDS Vaccine Initiative, the Global Alliance for anti-TB Drug Development, and the Medicines for Malaria Venture (summarised in Chapter 3 of the main report). **Additional public support could be usefully channelled through such public-private partnerships, subject to appropriate governance and accountability structures and monitoring of progress and outputs. Rationalisation of the existing proliferation of initiatives should be encouraged.**
- 13 Intellectual property issues are crucial in public-private partnership arrangements. It is important to strike the right balance of funding and risk between the public and private sector partners, so that the incentives for the private sector are sufficient without being larger than necessary. It is also critical to ensure that the price of any emerging product is affordable to the

⁺ Kettler (2000)

^{*} Widdus et al (2001)

end user. Public funds can be deployed to achieve this through appropriately structured patent arrangements.

Tax incentives for research and development

- 14 The public-private partnerships described above tend to use public funds to leverage additional private funds. Another approach is to use public funds to leverage private sector research and development activity. At the 'International Action Against Child Poverty' Conference in London on 26 February 2001, hosted by the Chancellor of the Exchequer (UK Finance Minister) and the Secretary of State for International Development, **the UK announced that it will provide tax credits for research and development on drugs and vaccines for the diseases of poverty.** We would urge others to make similar commitments to strengthen global incentives.
- 15 The UK tax credit will be additional to existing incentives, and to any further tax credits for research and development introduced following the consultation process announced in the Budget on 7 March 2001. Companies undertaking research into specified diseases will be eligible for an extra 50 per cent relief on qualifying expenditure. The Government plans to consult on the details of the new credit, the coverage of which will depend upon the response from the pharmaceutical industry. The Government will consider extending the credit to cover activity undertaken overseas by UK firms, although this will depend on assurances from the industry that it will respond to this wider coverage with genuinely new commitments (UK Budget 2001).

Establishing a clinical trials platform

- 16 Analysis by disease of products in the pipeline indicates a cluster of products in the stages prior to phase 3 clinical trials. Consultation with the pharmaceutical industry and public sector research institutions has revealed that the absence of an accessible clinical trials platform delays bringing new products through the later stages of testing and development, and might act as a disincentive to embark on basic research on new products.
- 17 Recognising this, and in the broader context of the European Commission's Programme of Action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction, the European Commission has proposed that a European Clinical Trials Platform be established to accelerate the development of new products for use in developing countries.⁺
- 18 The proposed clinical trials platform would facilitate networking and co-ordination of research; strengthen trials infrastructure in developing countries; and leverage funds to sponsor trials. It is envisaged that a core consortium of EC Member States would establish the platform and initiate operations, and would be joined by developing countries and development institutions. Eligibility would be restricted to appropriate trials, according to pre-determined criteria and a "peer review gate". Access could be based on a sliding scale of user fees for public research institutions, public-private partnerships, and private companies, regardless of global location. The platform's architecture would be limited, with a light central organisation (director and secretariat)

⁺ COM(2001)96, 21 February 2001

implementing the decisions of a governing body with full stakeholder representation. The central organisation might be eligible for EC funding; development of trials infrastructure and sponsorship of trials would be sought from public-private partnerships, development institutions, private companies and foundations.

- 19 There is a strong case for the establishment of a clinical trials platform along the lines proposed by the EC, subject to agreement that developing countries would play a leading role in its development and operation; that trials would be restricted to products to tackle diseases of poverty in developing countries, with initial priority given to HIV/AIDS, TB and malaria; and that access would be open to all appropriate products, without discrimination by global location or sector, but with application of suitable user fees. It is important that work to establish a clinical trials platform – EC led or otherwise – begins as soon as possible, so that new products emerging in the near future can be appropriately trialled without delay.

Harmonising the regulation of new products

- 20 Before new products enter use, they are subject to rigorous regulatory scrutiny to assess safety, quality and efficacy. The regulatory process varies between countries by approach, criteria, standards, capabilities and timeliness. This variation causes delay in universal product availability as companies phase their efforts to gain approval in different jurisdictions and because additional effort is sometimes required to meet different scientific or dossier requirements.⁺
- 21 New products to tackle HIV/AIDS, TB and malaria in developing countries are prone to the delays outlined above, particularly where products utilise new technologies, on which there is no international consensus on safety and quality. This delay in approval and licensing has a direct impact on the burden of disease, both by delaying the availability of new products and potentially acting as a disincentive to develop new products.
- 22 ***Recommendation: appropriate human and financial resources be set aside to speed-up product approval by regulatory bodies in developed and developing countries, and harmonise developing countries' requirements.*** In the first instance, agreement should be sort for new products to tackle HIV/AIDS, TB and malaria in developing countries.
- 23 The WHO is well-placed to co-ordinate activity to streamline approval procedures, although the authorities in developing countries will bear a disproportionate human and financial resource cost for which appropriate assistance will be required. It is important that work to harmonise regulations begins now, so that new products that emerge in coming years can reach those who need them without unnecessary delay.

⁺ Isbell and Widdus (2001)

Annex 6: Summary of the analysis: model overview and results

Introduction

1 The PIU has worked in conjunction with the Brookings Institution in a modelling analysis to provide quantitative estimates of the impact of the policy instruments highlighted in the report.

2 Market failures and poverty in countries where the burden of disease is highest has led to problems of access to existing products and under investment in the development of new technologies. A range of policy instruments, including an advance purchase commitment, a current purchase fund, intellectual property rights (IPR) buyouts, roaming exclusivity,⁺ a tax credit on R&D and direct government R&D have been assessed on the efficiency with which they address these market failures. Quantitative estimates of the number of disability adjusted life years (DALYs) saved through these interventions have been provided by using a behavioural model of R&D effort, a product cost effectiveness model and a current purchase fund model. These models have then been combined to estimate the impact of a global fund for health.

3 It should be recognised that there are significant uncertainties surrounding the effectiveness and arrival of new products and the extent to which health care systems can make use of existing and new technologies. The figures reported in this model should be used only as a guide to the scale of resources that are needed to combat these diseases and help frame consideration of alternative policy options.

Section 1: Model Properties

- 4 The behavioural model of R&D begins with the observation that the expected arrival of any new product depends on both the quantity and quality of projects pursued by the pharmaceutical industry. The total R&D effort expended in the pursuit of new products will depend on the private value of the market to the firm, the expected costs incurred by the firm and the probability of success of each project that can be pursued. Policy interventions that either increase the market size for new technologies (pull programs) or reduce the costs faced by the pharmaceutical industry (push programs) will increase the number of projects pursued reducing the expected time of arrival for new products. The behavioural model of R&D effort and the product cost effectiveness model examines how each of the policy instruments affects the pharmaceutical industry's investment appraisal decisions. This includes estimating the median time in bringing new drugs and vaccines to market, the expected number of DALYs saved, the total expected cost to the global public sector and the impact of making new technologies affordable in developing countries. The assumptions in the model recognise that there is a significant probability that more effective technologies suitable for use in developing countries (such as

⁺ The extension of an alternative patent held by the pharmaceutical company.

vaccines) will not be developed due to difficulties in solving the scientific problems. The sensitivity analysis considers the impact of varying the underlying assumptions in the model.

- 5 Access to health technologies encompasses a wide range of factors of which affordability is one of the key components. Other considerations such as improving infrastructure and health delivery systems are not modelled explicitly here and are conservatively assumed to remain at a similar level to today. The cost effectiveness model explicitly addresses coverage rates of new technologies and the co-payment levels required by developing countries. From this the increased social surplus generated by interventions that address affordability in developing countries are estimated.
- 6 The cost effectiveness of currently available technologies are covered in a number of ways. Certain products such as Nevirapine and Antiretrovirals are modelled explicitly taking into account such factors as mother to baby transmission levels. A more generalised model has also been developed in order to give estimates for the effectiveness of the numerous other products which, owing to the time-scale of the project, could not be modelled individually. Finally we have derived estimates of the cost effectiveness of non-pharmaceutical technologies such as bednets and condoms from surveys conducted by The Asian Development Bank and The Global Forum for Health Research. This information has been used to estimate the impact of a current purchase fund by constructing a linear model of expenditure and expected DALYs saved.
- 7 The behavioural and current purchase fund models were then merged in order to estimate the impact of the global fund for health. This deals directly with the interaction between the current and advance sections of the fund explicitly modelling how a current fund may be used to increase incentives for R&D and may purchase new products once they have been developed.
- 8 In order to calculate the necessary outputs from the models we are required to make certain assumptions about the state of science and existing market sizes. A full assessment of the assumptions used in the model can be found in a PIU working paper on the model analysis that will shortly be available.

Section 2: Summary of results

- 9 Our sensitivity analysis on the underlying assumptions of the model shows that there is considerable variation in the model results. As such we do not recommend drawing precise figures from the results, rather that they should be used to give an estimate of the scale of resources required.
- 10 The behavioural model considers the cost effectiveness of an advance purchase commitment, an intellectual property right (IPR) buyout, roaming exclusivity, direct government R&D and a tax credit on R&D. The results suggest that an advance purchase commitment is the most cost-effective method of inducing the development of new products. Inducing a new vaccine for each disease with a median time of arrival in 10 years would save an estimated 1.1 billion additional DALYs at an expected cost per additional DALY of \$1.24 for an HIV/AIDS vaccine, \$3.46 per additional DALY for a Malaria vaccine and \$3.75 per additional DALY for a TB vaccine.

- 11 The current purchase fund model show that an annual commitment of \$1 billion for 20 years would save an estimated 650 million DALYs. Of this 310 million DALYs would be in HIV/AIDS, 260 million would be in malaria and 80 million would be in TB. Further the analysis highlights the reduced cost-effectiveness from purchasing expensive treatment drugs such as antiretrovirals as opposed to cheaper preventative products.
- 12 On our central assumptions the results of the global fund for health show that a fund of \$30 billion (£10 billion advance, \$20 billion current) over 20 years would save an estimated 1,520 million DALYs by 2010. Of which 610 million DALYs would be in HIV/AIDS, 350 million DALYs in malaria and 560 million DALYs in TB equivalent to 50 million lives⁺. Increasing the resources in the global fund increases the impact on DALYs saved however, altering the balance between the current fund and the advance purchase commitment brings different benefits (see below). An illustrative example of the sensitivity analysis carried out for Malaria is shown below in Box 1.

⁺ Lives of a 30 year old. See Murray and Lopez (1996)

Box 1: Malaria Sensitivity Analysis

The sensitivity analysis was conducted by varying the assumptions in the model by plus and minus 10%. The results of the sensitivity analysis are shown below:

Table 1 Expected number of DALYs saved by 2010

Total size of commitment	Current (\$billion)	Advance (\$billion)	Malaria assumptions -10% (DALYs million)	Malaria central assumptions (DALYs million)	Malaria assumptions +10% (DALYs million)
20	10	10	160	300	360
30	20	10	210	350	410
50	40	10	310	450	510
70	60	10	410	550	610
20	10	20	190	370	450
30	10	40	210	430	520
50	10	60	220	460	560

Variation in the current purchase fund is more robust to changes in the underlying assumptions than variation in the advance purchase commitment. The range of values reported is large with the more negative assumptions halving the effectiveness of the fund for some configurations. Diminishing returns to scale mean that increasing the assumptions bring about a smaller increase in the number of DALYs saved.

The sensitivity is such that it is not possible to draw precise estimates from the model. The values reported should be used only as an estimate for the general scale of impact that a given level of resources might achieve.

- 13 Within a global fund for health altering the balance of expenditure between the current purchase fund and the advance purchase commitment alters the number of DALYs saved. Figs 1 and 2 below show the impact of altering each section of the global fund while holding the other constant.

Figure 1: Global Fund for Health DALYs saved holding current fund constant

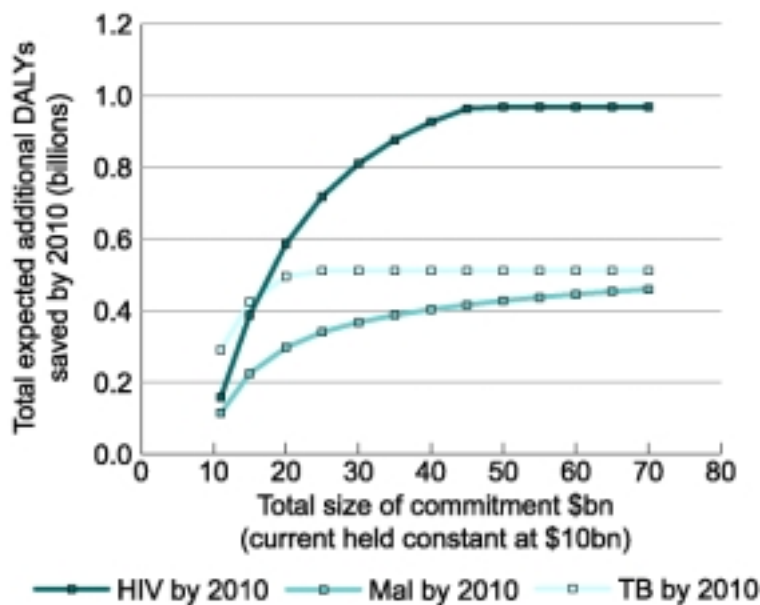
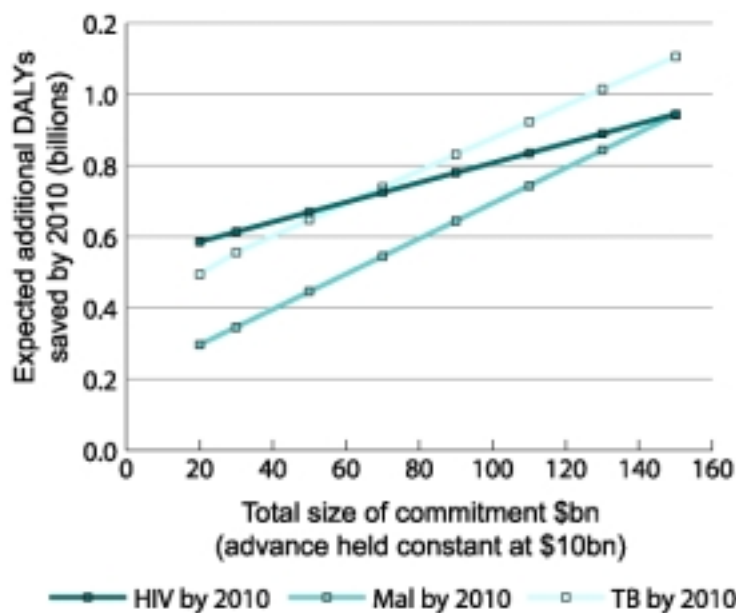


Figure 2: Impact of Global Fund for Health, holding Advance Constant



- 14 Initially increased spending on the advance purchase commitment brings about larger gains than spending on the current purchase fund but the impact is not linear. The assumptions in the model mean that it is initially more cost-effective to bring forward the arrival of new technologies. However, the limits to the intensity of effort from increased spending on R&D means that there is very little gain from increased spending beyond \$20 billion for malaria and TB and \$40 billion for HIV/AIDS. This factor combined with the large uncertainties surrounding the advance purchase commitment (see Box 1) suggest devoting approximately one third of the total global fund for health to increasing the incentives for new products.
- 15 Our analysis has shown that in order to have a significant impact on the prevalence and incidence of HIV/AIDS, malaria and TB over the coming decade there needs to be a step-change in the level of resources invested by

the international community. Given the uncertainties surrounding these figures it may be necessary to scale-up the level of resources committed over time to meet any increasing threat posed by these diseases.

Glossary of terms

DALY – (Disability Adjusted Life Year) A unit used for measuring both the global burden of disease and the effectiveness of health interventions, as indicated by reductions in the disease burden. It is calculated as the present value of the future years of disability-free life that are lost as a result of the premature deaths or cases of disability occurring in a particular year (World Bank, 1993)

Deadweight Loss – A loss in social welfare deriving from a policy or action that has no corresponding gain.

Delivery System – The ability of a nation's health care system to deliver available technologies to its population.

Differential pricing – See Tiered Pricing.

Drug – Any chemical compound that is used in the prevention, diagnosis, treatment, or cure of disease, for the relief of pain, or to control or improve any physiological or pathological disorder in humans or animals.

Effective Demand – The level of demand reflected by the ability to purchase goods through the pricing structure.

Epidemic – Defined by a rate of transmission greater than 1.

Gaps – Missing technologies or action.

Gold Plate – Over capitalisation in non-innovative areas.

Interventions – Any form of government interference with market forces to achieve economic ends.

Incidence (of disease) – The rate of new infection.

IPR – Intellectual Property Rights.

Low Technology Solution – Non-pharmaceutical technologies such as condoms and bed nets that can prevent incidence of disease.

NGO – Non Governmental Organisation.

Parallel Trade – A flow of imports from a low price to a high price country in addition to the normal flow of imports generated by manufacturers and traders (arbitrage).

Policy Instrument – A form of government intervention designed to increase efficiency or equity. See also Push, Pull & Regulatory instruments.

Push Instruments – Instruments that directly stimulate R&D early in the timeline.

Pull Instruments – Instruments that indirectly stimulate R&D by increasing the value of the prospective market.

Prevalence (of disease) – The level of infection.

R&D Timeline/Pipeline/Process – The development profile of a new technology.

Regulatory Instruments – Instruments that indirectly stimulate R&D by providing a better framework for agents to operate in.

Stakeholders – Organisations that have a vested interest in the work carried out in the project. Stakeholders are organised into three levels: Primary Stakeholders (people and organisations directly affected by outcomes of the project), Secondary

Stakeholders (people and organisations who can influence the outcome of the project) and Tertiary Stakeholders (organisations that have an interest in, but no direct influence on, the work carried out in the project).

Technology – Any device or treatment that can prevent and/or cure disease.

Tiered Pricing – Also referred to as differential pricing. The sale of the same commodity to different buyers at different prices.

TRIPS – Trade Related Intellectual Property Rights.

Vaccination – Process of inoculating a host with microbial antigen(s) to elicit specific immunity.

Vaccine – 1. Immunology: a preparation, consisting of killed, pre-treated, or living micro-organisms or molecules derived from them, that is used in vaccination.
2. Virology: specifically, a suspension of attenuated or killed viruses that are administered to vertebrates to produce immunity to that viral infection.

People consulted for this project

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5th meeting of the WHO Commission on Macroeconomics and Health, Addis Ababa, March 2001

Intellectual Property Rights and Global Health Challenges for Access and R&D a joint meeting of the Wellcome Trust and the Commission on Macroeconomics and Health

Useful website addresses

The Joint United Nations Programme on HIV/AIDS

<http://www.unaids.org>

International AIDS Vaccine Initiative (IAVI)

<http://www.iavi.org>

Roll Back Malaria

<http://www.rbm.who.int>

Malaria Vaccine Initiative

<http://www.malariavaccine.org>

STOP TB

<http://www.stoptb.org>

Global Alliance for TB drug development

<http://www.tballiance.org>

The World Health Organisation

<http://www.who.int>

MSF Access to Essential Medicines

<http://www.accessmed-msf.org>

Global Alliance for Vaccines and Immunisations (GAVI)

<http://www.vaccinealliance.org>

Medecins sans Frontieres

<http://www.msf.org>

Oxfam International

<http://www.oxfam.org>

The World Bank

<http://www.worldbank.org>

Global Forum for Health Research

<http://www.ippph.org>

The World Intellectual Property Organisation

<http://www.wipo.int>

The Association of the British Pharmaceutical Industry

<http://www.abpi.org.uk>

International Federation of Pharmaceutical Manufacturers Association

<http://www.ifpma.org>

Pharmaceutical Research & Manufacturers of America

<http://www.phrma.org>

The Bill and Melinda Gates Foundation

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The Rockefeller Foundation

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UK Department for International Development

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