Parliamentary Office of Science and Technology

postnote

**July 2001** Number 160

# ACCESS TO MEDICINES IN THE DEVELOPING WORLD

**Access to pharmaceuticals, such as anti-HIV drugs, in the developing world has attracted much recent attention. It was discussed by the Council of the World Trade Organisation (WTO) in June 2001 and has been the subject of trade disputes, a high profile legal case, and campaigns by charities such as Oxfam. This briefing outlines the international intellectual property (IP) regime and examines options through which developing countries can access effective treatments.**

## Background

Estimates for the year 2000 suggest that HIV/AIDS, tuberculosis (TB) and malaria were responsible for some five million deaths world-wide. Developing countries bear a disproportionate burden of death and illness caused by such diseases. For instance, in recent years HIV/AIDS has become highly prevalent across sub-Saharan Africa, where it is estimated to have already caused 2.4 million deaths; a further 25.3 million people in the region are HIV positive.

Such diseases may be treated with modern drugs. For instance, people with TB can be readily treated with a combination of anti-bacterial drugs, although treatment courses are long (even current short treatment courses take 6-8 months). While there is no cure for AIDS, modern anti-HIV drugs can delay the onset of the disease and prevent infections such as TB, the leading infectious killer of people with HIV/AIDS. Anti-HIV drugs work by blocking various stages of the lifecycle of the virus (see box opposite) and are most effective when two or three are given in combination. In developed countries the preferred treatment is triple 'combination therapy', which is taken for a lifetime and can involve complex drug regimes. Patients also need to be monitored using sophisticated diagnostic tools.

### Anti-HIV Therapy

Anti-HIV drugs have been widely used in developed nations since the launch of AZT in 1986. Three different classes of drug are available (see POSTnote 118 for more details). Two of these classes of drug work by inhibiting a viral enzyme (reverse transcriptase) used to copy HIV genes in the host cell. The third class inhibits another viral enzyme (HIV protease) needed to assemble new virus particles.

When anti-HIV therapy was first used and tested, patients were prescribed a single type of drug (monotherapy). This resulted in clear benefits, but the effects were transient - it became clear that HIV was developing drug resistance. Monotherapy has now been replaced by combination therapy in which two or three different classes of anti-HIV drugs are given together. This is based on the idea that even if a strain develops resistance to one drug, it will still be susceptible to the others. Triple combination therapy reduces viral load to below detectable levels in some 70-80% of patients, but requires high-level patient support and commitment. For instance, sophisticated diagnostic techniques are needed to monitor viral load and the state of the patient's immune system. Combination therapy can cause multiple side-effects; the number of drugs involved (up to 20 pills a day) and the fact that some may need to be taken with water, others on a full stomach, etc. also make for complex drug regimes. Failure to adhere to a drug regime can lead to the emergence of drug resistant strains, which may in turn limit future therapeutic options.

## Drug patents and the TRIPS agreement

### Generic drugs

Many of the drugs used to treat such diseases – particularly the anti-viral drugs used in HIV/AIDS therapy - are still under patent. A patent provides the owner of an invention with the legal means to prevent others from selling it for a period of 20 or so years. In return, the patent holder must disclose details of the invention. The

exclusivity provided by a patent allows pharmaceutical companies to recoup their investment[1] in developing a new medicine. Once the patent expires on a drug, other manufacturers are free to step-in and manufacture so-called **generic** versions of the drug. In some countries (e.g. India) which do not yet have (or do not recognise) patent regimes covering pharmaceuticals, manufactures also make generic versions of in-patent drugs. Generics are usually far cheaper than in-patent drugs since generic manufacturing is a competitive business and the companies do not have to worry about recovering research and development (R&D) costs. Thus, whereas triple combination therapy for HIV/AIDS costs ~£10,000 per person per year in the developed world, generic versions of the same therapy are available for as little as £250 per person per year.

### TRIPS

The Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement was a result of the 1986-94 Uruguay Round of multilateral trade negotiations. It aims to harmonise the way IP is protected around the world by setting common international rules designed to protect the rights of innovators while providing maximum access to innovations. The World Trade Organisation (WTO) administers TRIPS through the TRIPS Council, which consists of all WTO members and includes a system for the settlement of disputes between member nations.

TRIPS came into effect on 1 Jan 1995. Developed, developing and 'least developed' countries were given 1, 5 and 11 years respectively to ensure existing legislation was compliant. Where countries did not have patent protection for a particular area of technology (such as pharmaceuticals) TRIPS allowed up to 10 years (by 2006) to introduce it. Introduction of TRIPS-compliant IP regimes could threaten the generics industries in countries like India. However, as outlined in the box opposite, TRIPS contains two 'get-out' mechanisms that allow countries to manufacture (compulsory licensing) or buy (parallel importing) in-patent products such as generic drugs in exceptional circumstances. But, as discussed in the following section, neither mechanism has proved easy to use in practice.

## Trade disputes

Recent years have seen a number of trade disputes and/or legal actions involving pharmaceuticals. Some of these have involved the US using Section 301 of its 1974 Trade Act. As outlined in the box opposite, this is effectively a list of countries that may incur trade sanctions because the US considers them to be infringing drug or other patents. Two recent cases – in South Africa and Brazil (see box on page 3) – illustrate the complexity of the issues arising from such disputes. Both cases were triggered by attempts to introduce new laws which were supposedly WTO/TRIPS-compliant. In both cases the laws have subsequently been challenged on the grounds that they contravene WTO patent rules. As discussed in more detail in the next section, this has led to suggestions that there is a need for clarification or even reform of the TRIPS agreement.

### TRIPS exemptions

While the TRIPS agreement is designed to protect IP rights around the world, it contains mechanisms allowing countries to vary such rights under certain circumstances.

**Compulsory licensing (CL)** – TRIPS allows governments to permit use of a patent without the consent of the owner in certain circumstances, for example:

- where a company/person has already attempted to gain a voluntary license from the patent holder on reasonable commercial terms;
- or in the event of 'national emergencies' or 'other circumstances of extreme urgency';
- or for 'public non-commercial use'.

Compulsory licenses can only be issued if adequate remuneration is paid to the patent holder, exclusivity is not given to a single licensee, and production is mainly to supply the domestic market.

**Parallel importing** refers to products marketed by the patent owner in one country and imported into another without the patent owner's approval. It occurs where there are price differences for the same goods in different markets, as is often the case for pharmaceuticals. Generally, once a company has sold its product, its patent is 'exhausted' and it no longer has any rights over what happens to the product. TRIPS is 'neutral' on parallel imports, simply stating that none of its provisions can be used to address this legal principle of 'exhaustion'.

### The US Section 301 Watch List

Section 301 of the 1974 Trade Act allows the US to employ measures against any country that it considers:

- is denying US companies or persons adequate and effective protection of their IP rights;
- has an IP regime that denies US companies or persons fair and equitable market access.

Section 301 was amended following the Uruguay Round of trade negotiations; a country can be found to deny adequate and effective intellectual property protection even if it is in compliance with its obligations under TRIPS. US retaliation under Section 301 includes suspension of trade agreements or the imposition of duties or other import restrictions.

## TRIPS-related issues

### Reform or clarification?

The cases outlined in the box on page 3 illustrate some of the difficulties faced by developing countries in trying to use TRIPS safeguards such as compulsory licensing and parallel importing. Indeed, neither of these safeguards has yet been used successfully by a developing nation to access inexpensive medicines. Among the likely reasons for this are:

- fear of bilateral trade disputes;
- lack of legal resources to interpret and implement the agreement;
- lack of the infrastructure needed to dispense drugs;
- the implications of declaring a 'national emergency' (e.g. damaging international perceptions).

Such factors raise the question of whether TRIPS needs wholescale reform, or merely further clarification. Non-governmental organisations (NGOs) such as Oxfam argue

### Key trade/legal disputes

**South Africa**

In 1997, South Africa introduced the Medicines and Related Substances Control Amendment Act Number 90. This was intended to provide a legal framework for its national drugs policy. The Act allowed the Government to override patent rights in the pharmaceutical sector on public health grounds. It appeared that this would allow the Health Minister to permit the use of parallel importing and compulsory licensing. This legislation led the US to place South Africa on its 301 Watch List and filed a complaint against South Africa with the WTO. It also led to a legal action against the South African Government by some 40 drug companies, which argued that the new law conflicted with the South African constitution and contravened WTO patent rules.

The case aroused considerable public and media interest. In December 1999, the US stopped its action stating that it was committed to helping developing countries gain access to essential medicines. In April 2001 the drug companies withdrew their case when the South African Government reaffirmed its commitment to honour TRIPS and the parties agreed to work together to implement the legislation. While the outcome of this dispute has been portrayed as a moral victory for South Africa and for HIV/AIDS campaigners, it is by no means clear that the South African government ever intended to use the proposed new law to provide anti-HIV drugs. Indeed, the South African Government has questioned the link between HIV and AIDS. The Health Minister has also stated that South Africa could not afford to use the drugs even if they were available free of charge, due to the high cost of distributing, administering and monitoring their use. Any new law is most likely to be used to buy drugs to combat infections such as TB which are closely linked with HIV infection.

**Brazil**

In 1997, Brazil introduced a patent law it considers TRIPS-compliant. The law included pharmaceutical products within its scope. It requires all patent owners to manufacture their patented products in Brazil or be subject to compulsory licensing. The US has questioned whether the law is TRIPS-compliant; it has placed Brazil on its Section 301 Watch List and started proceedings under the WTO dispute system (although this action was withdrawn in June 2001).

Again, in public opinion this trade dispute has been linked with access to anti-HIV drugs. The Brazilian Government funds a programme providing anti-HIV therapy to over 90,000 people. Most of the drugs are produced locally; the Brazilian Government is concerned that a trade dispute may jeopardise this programme if it is forced to use more expensive drugs. The US considers the new law discriminates in favour of locally produced products, and suggests that Brazil could use other provisions in its patent law to compulsory license drug patents.

that there is a need for clarification of the terms within TRIPS but also consider revision of the Agreement is required. Oxfam has recommended the WTO to:

- impose a moratorium on trade disputes with developing countries over TRIPS-compliance;
- conduct a review of the impact of TRIPS;
- outlaw the use, or threatened use, of bilateral trade sanctions for enforcing potentially 'harmful' levels of IP protection (such as the US 301 provisions).

The UK Government considers that, overall, TRIPS provides an appropriate balance between allowing access to inventions on the one hand and encouraging research and development on the other. It agrees that clarification of terms within the Agreement is needed and has set up a commission on intellectual property rights to consider how national IP regimes can best be designed to benefit developing countries, within the context of existing international agreements such as TRIPS.

On 20 June 2001, the TRIPS Council held a special meeting on IP and access to medicines, at the request of African members of the WTO. According to the WTO's unofficial summary[2] of the meeting, there was general agreement that patents are necessary as an incentive to invent and develop new drugs. But it was also recognised that the 'flexibilities' contained in TRIPS required clarification and that the Agreement itself may possibly need amending. For instance, justification for compulsory licensing may need clarification since the TRIPS agreement does not set out all possible circumstances under which governments may grant such licences. It is however, widely agreed that the HIV/AIDS epidemic in sub-Saharan Africa meets one of the criteria mentioned in TRIPS ('a national emergency'). The meeting agreed that:

- the WTO secretariat will compile a 'checklist' of all the relevant TRIPS provisions and the issues identified in connection with them;
- the TRIPS Council will hold an informal meeting on 25 July 2001 to discuss the checklist;
- the issues will be discussed at the next formal TRIPS Council meeting on 19 September 2001.

## Affordable medicines

Reducing the price of medicines in developing nations has emerged as a major priority in recent months. This could be achieved by a variety of different mechanisms. Some of these may involve clarification of the TRIPS agreement, whereas others are more concerned with agreements between individual companies and governments.

*Manufacture of drugs under compulsory licensing*

TRIPS currently stipulates that products made under compulsory licences should be 'predominantly for the domestic market'. This is fine for those developing countries such as India with an established generics industry that can use compulsory licensing as a means of achieving technology transfer as well as improving access to medicines. But clarification may be needed to ensure that this stipulation does not prevent developing countries using compulsory licences to export affordable drugs to other developing countries that do not have a generics industry.

*Voluntary licensing*

Voluntary licensing involves an agreement being reached between a licensee and a patent holder for the licensee to produce a patented product without infringing patent rights. The UK Government has recommended that WTO explore ways in which voluntary licensing could be made more widespread and effective as a means of improving access to medicines.

*Parallel importing*
An alternative to developing countries making their own copies of drugs under licence is for governments to import drugs from elsewhere. Procurement of cheap drugs on the open market (parallel importing) is clearly[2] allowed under TRIPS although attempts to use this as a means of accessing affordable medicines have led to trade disputes in the past. Further clarification of WTO rules may be required to ensure that developing countries using parallel importing to access affordable medicines do not face trade sanctions from developed nations.

*Differential pricing*
Differential pricing is where pharmaceutical companies make and sell the same drug at different prices in different markets. Pharmaceutical companies stress the need to differentiate drugs for different markets (e.g. by changing the packaging) and for governments to provide effective trade regulation preventing re-importation into developed countries. A number of companies have already offered cheap anti-HIV drugs either through the UNAIDS 'Accelerated Access Initiative' (AAI, launched in May 2000) or through other initiatives. AAI brings together a number of companies that have pledged to supply cut-price anti-HIV drugs to developing countries. Prices negotiated through the scheme vary, but are thought to be in the region of $1,000 (~£700) per patient per year for triple therapy. In May 2001, the UK Government proposed a framework be put in place to facilitate differential pricing of patented products. While welcoming initiatives such as the AAI, groups such as Oxfam and Medecines sans Frontieres (MSF) stress that further measures are needed to reduce costs in developing countries, noting that:

- Progress under AAI has been slow, largely because it involves negotiating with individual governments. Indeed one of the companies (Merck & Co) recently announced it was abandoning country-by-country negotiations under AAI and simplifying the process by offering a single price to all developing countries.
- Price reductions achieved under AAI (which delivers triple combination therapy for ~$1000 per patient per year) are not as great as those offered by generics (the cheapest comparable price is currently ~$350, close to the target affordable price of $200 identified by MSF). Oxfam considers such initiatives work best where there is competition from generic companies.
- AAI applies to anti-HIV drugs – similar initiatives are needed to improve access to drugs for other diseases.

## Other mechanisms

Improving access to medicines is not just a matter of making medicines more affordable. Agencies such as the World Health Organisation (WHO) see three other essential requirements for improving access.

**Rational selection**
Governments are encouraged to draw up national lists[3] of essential medicines from WHO's Essential Drugs List, which outlines safe, effective treatments for the vast majority of diseases of most concern in developing countries. Around 95% of the drugs on this List are available as generics. Apart from limited short-term usage (e.g. to prevent mother to child transmission), the WHO has excluded anti-HIV drugs from the List because of insufficient evidence that they can be used in 'resource poor healthcare situations'. However, groups such as Medecins Sans Frontieres have called for the List to be compiled more on the basis of medical need rather than on considerations of cost-effectiveness.

**Sustainable financing**
WHO encourages developing countries to establish sustainable funding mechanisms for healthcare delivery – for instance from government revenues or social health insurance. Financing healthcare systems also requires agreements between development agencies and governments. WHO recently called[4] for the establishment of a new international health fund to allow money to be transferred rapidly to countries most at need, while maintaining accountability and transparency. WHO has stressed such mechanisms must ensure that decision making and priority setting remain at national level.

**Healthcare infrastructure**
Governments also need to invest in the basic healthcare infrastructure to distribute, store and dispense drugs and to monitor patients (particularly for anti-HIV drugs). Facilitating the development of reliable supply systems is thus a major strand of WHO's Medicines Strategy. In practice, this involves encouraging governments to provide certain minimum standards of healthcare (e.g. the provision of clinics within one hour's travel).

## Research

Most R&D into new medicines is aimed at the diseases affecting developed countries. The UK Government and NGOs agree that protection of intellectual property alone is insufficient to encourage R&D investment on the diseases of poverty. This is because research decisions are driven by the expected return on investment, which includes the size of the market and the ability of the customer to pay. They also agree that there should be additional public funds (Oxfam has proposed a $5 billion international fund) targeted towards research for tackling the diseases affecting developing countries. The UK Government recently announced a number of measures to encourage such research, including targeted public support for research on HIV/AIDS, TB and Malaria as well as tax credits for R&D on drugs and vaccines.

**Endnotes**

1 The pharmaceutical industry estimates that it takes 10-12 years and costs ~£350M to develop a new drug.
2 http://www.wto.org/english/tratop_e/trips_e/counciljun01_e.htm
3 160 countries now have national drugs lists.
4 http://www.who.int/director-general/speeches

POST is an office of both Houses of Parliament, charged with providing independent and balanced analysis of public policy issues that have a basis in science and technology. POST would like to thank Dr Amanda Collis for her assistance in the preparation of this briefing note

The Parliamentary Office of Science and Technology, 7 Millbank, London SW1P 3JA Tel 020 7219 2840

**www.parliament.uk/post/home.htm**