

## Access to AIDS medicines stumbles on trade rules

Developing countries have several international trade law provisions at their disposal to help them buy life-saving medicines at affordable prices for public health needs, particularly HIV/AIDS. But only a few countries are using these because of red tape and political pressure. WHO is helping countries navigate the procedural maze.

Developing countries are failing to make full use of flexibilities built into the World Trade Organization's (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to overcome patent barriers and, in turn, allow them to acquire the medicines they need for high priority diseases, in particular, HIV/AIDS.

First-line antiretroviral (ARV) drugs for HIV/AIDS have become more affordable and available in recent years, but for patients facing drug resistance and side-effects, second-line ARV drugs and other newer formulations are likely to remain prohibitively expensive and inaccessible in many countries. The problem is that many of these countries are not using all the tools at their disposal to overcome these barriers.

Medicines protected by patents tend to be expensive, as pharmaceutical companies try to recoup their research and development (R&D) costs. When there is generic competition prices can be driven down dramatically.

The TRIPS Agreement came into effect on 1 January 1995 setting out minimum standards for the protection of intellectual property, including patents on pharmaceuticals. Under that agreement, since 2005 new drugs may be subject to at least 20 years of patent protection in all, apart from in the least-developed countries and a few non-WTO Members, such as Somalia.

Successful AIDS programmes, such as those in Brazil and Thailand, have only been possible because key pharmaceuticals were not patent protected and could be produced locally at much lower cost. For example, when the Brazilian Government began producing generic

AIDS drugs in 2000, prices dropped. AIDS triple-combination therapy, which costs US\$ 10 000 per patient per year in industrialized countries, can now be obtained from Indian generic drugs company, Cipla, for less than US\$ 200

per year. This puts ARV treatment within reach of many more people.

Several newer AIDS drugs and formulations of existing drugs are urgently needed in developing countries but are not available because pharmaceutical companies are choosing not to sell them, and no generic versions of these are available.

For example, there is a new formulation of the ARV combination therapy lopinavir/ritonavir, which unlike its predecessor does not need refrigeration. This would be useful in Africa, where temperatures are high and electricity supplies irregular,

but Médecins Sans Frontières (MSF) says it is not available there at all.

Another example is Gilead Sciences' Tenofovir, a brand-name drug which has significantly fewer side-effects than some older ARVs and was added to WHO's list of prequalified medicines, recommended for UN agencies to purchase for use in developing countries. Tenofovir is, however, virtually unavailable in Africa although it can be an effective second-line ARV, according to Ellen 't Hoen, Director of Policy and Advocacy at MSF. Most AIDS patients eventually need to switch to second-line treatment because of side-effects and drug resistance. However, according to MSF, while the US company has announced a price of US\$ 208 per person per year in 97 countries, the product is only registered in 10 of those. Many developing countries cannot pay the normal price for this drug. For example, in Brazil it is US\$ 2600 per patient per year and that is the price for just one of three drugs in combination treatment.

Following the TRIPS Agreement, there was growing concern and evidence that patent rules might restrict access

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*Cecilia Oh, from WHO's Department of Technical Cooperation for Essential Drugs and Traditional Medicine.*



Women in front of a campaign poster that reminds people with HIV/AIDS in Botswana that they must take antiretroviral (ARV) medicines for the rest of their lives. Botswana is one of the few countries in sub-Saharan Africa that provides more than half of its people with HIV/AIDS with life-saving ARV treatment.

WHO/E. Miller

to affordable medicines for people in developing countries, particularly for HIV/AIDS, tuberculosis and malaria. This led to the November 2001 Doha Ministerial Declaration which stated: “The (TRIPS) Agreement can and should be interpreted and implemented in a manner supportive of WTO members’ right to protect public health and, in particular, to promote access to medicines for all.” The Declaration refers to a number of flexibilities, including the right to grant compulsory licences and to permit parallel importation (see box). It also extends the transition period during which least-developed countries do not have to enforce or grant patents on pharmaceutical products until 2016.

However, countries have been slow to review their patent laws to make the most of the flexibilities within the TRIPS provisions.

Cecilia Oh, from WHO’s Department of Technical Cooperation for Essential Drugs and Traditional Medicine, tells the *Bulletin*: “Developing countries are not moving fast enough to put in place the legal framework and systems to ensure they have access to affordable medicines in the future.”

Oh adds: “There is a need for a better understanding of how the TRIPS flexibilities can be used to achieve public health benefits. In the case of ARVs, there may be a lack of urgency at the moment as most first-line ARVs are not affected, but these second-line drugs will be. We saw prices of first-line ARVs being dramatically reduced, largely because of competition from generics, but if we don’t have a strategy for ensur-

ing generic competition for second-line drugs then prices may stay high”.

One common misconception is that TRIPS requires a country to declare a national emergency before invoking a compulsory licence. Countries are free to determine the grounds for granting compulsory licences, such as broad public health interests. Neither does TRIPS bar countries with limited capacity from using parallel imports to bring in drugs that have been sold at a lower price in another country.

There are a few examples of countries that are making use of the TRIPS flexibilities, and the number is growing. For example, Zimbabwe declared a period of emergency in May 2002 over its AIDS epidemic, authorizing the government to override patents to permit the local production or import of ARV medicines. In October 2003, Malaysia allowed the import of generic didanosine, zidovudine and the lamivudine/zidovudine combination from India to supply its public hospitals, under the government use provision in its patent law. In March 2004, Mozambique granted a compulsory licence for local manufacture of a first-line triple-combination ARV. Zambia issued a compulsory licence, in September 2004, to permit the local production of first-line ARV therapy. Indonesia, in 2004, authorized government use of patents to enable local production of nevirapine and lamivudine. Some least-developed countries now allow the import and use of generic medicines, referring to their right under paragraph 7 of the Doha Declaration not to grant or enforce pharmaceutical product patents until at least 2016.

In South Africa and, more recently, Kenya, voluntary licences were agreed between local manufacturers and the patent-holding companies for the production of ARVs. Although technically these were voluntary, they were only agreed upon following heavy pressure from the government, civil society organizations and local manufacturers.

Sisule Musungu, from the South Centre, and Oh, from WHO, state: “A widespread lack of clarity about the options available, coupled with the lack of local legal and technical expertise to incorporate and implement TRIPS flexibilities in national law and policy are the obvious and major problems.”

WHO’s Department of Technical



The 3 by 5 campaign has spurred new global momentum to achieve universal access to ARV drugs by 2010.

WHO

Cooperation for Essential Drugs and Traditional Medicine has produced a series of technical documents to help countries understand how TRIPS flexibilities can be used. It has also organized meetings and regional workshops to bring together health ministries, patent offices, and trade and industry people to help them work together to develop a common policy. Cecilia Oh says: “One big problem is that often health and procurement people have little information about intellectual property and patents. As a result they are hesitant to act. It is important that all relevant government agencies, health, trade and patent agencies consult with each other.” Musungu says the work carried out by this small WHO department is useful, but more help is needed. “Much greater attention should be paid to the whole issue of intellectual property rights at the very top level of the World Health Organization.”

Developing countries that produce lower cost generics and attempt to bring down the price of medicines feel that they are under pressure from industrialized countries and the multinational pharmaceutical industry and tend to be reluctant to make the most of these provisions: “Following the Doha Declaration countries can legally set patents aside, but countries are hesitant to do so because they are afraid of provoking the anger of the United States. The political pressure is enormous,” says ’t Hoen: “I am worried that things will have to get a lot worse before countries make a move to ensure production through compulsory licences.”

The Brazilian case highlights the difficulties that countries can face. Brazil has a strong generics industry that supplies 40% of all ARV drugs used in the country. Brazilian law requires the patent holder to manufacture the product in Brazil and if this does not happen, the government can issue a compulsory licence to another producer.

### Compulsory licences

Compulsory licences allow third parties to use an invention without the patent holder’s consent. For example, local pharmaceutical companies may obtain compulsory licences to produce generic versions of patented medicines or to import generic versions of medicines from foreign manufacturers.

### Parallel import

Parallel import is the import and resale in a country without the consent of the patent holder of a patented product that has been legitimately put on the market of the exporting country. This means that drugs sold at a lower price in one country can be imported into another country where the same drug is sold at a higher price.

Both provisions are well within the parameters of the TRIPS Agreement. Brazil came under tremendous pressure from the United States — which filed a complaint to the WTO which it later withdrew — first to drop the law and later not to use it. Although Brazil was able to successfully stand up to that pressure, smaller countries may have found the pressure too great and given in. Brazil has, however, not so far issued a compulsory licence to produce second-line ARVs, placing a potential strain on national AIDS funds, 't Hoen says.

Although existing provisions of the TRIPS Agreement permit the granting of compulsory licences to enable generic production of medicines, countries without domestic manufacturing capacity cannot use this flexibility. This

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is because TRIPS requires production under compulsory licence to be predominantly for the supply of the domestic market. In 2003, the WTO waived this export restriction and

the decision is in the process of being made permanent. Under this waiver, countries that do not have their own drug manufacturing capability can issue a compulsory licence so that another country or company in another country can manufacture generic drugs for them.

However, organizations such as MSF have criticized the import mechanism for being unnecessarily cumbersome as it is based on a drug-by-drug, country-by-country and case-by-case decision-making process.

Under the waiver, potential exporting countries must amend their

national laws to enable the production and export of generic medicines under compulsory licence. Canada, India, China and Norway have done this while the European Union is considering draft legislation. But so far not a single product has been delivered to a patient under these new rules and no single country has even notified the WTO of its intention to use the system as an importer. This may be because it is too complex and burdensome.

WTO Members recently agreed to convert this system into an amendment of the TRIPS Agreement. The amendment is expected to come into force in 2007, if two-thirds of WTO Members ratify it.

Oh says: “Perhaps countries don't fully understand the system yet. Also at the moment manufacturers in India are still producing drugs that are not under patent. But in two to three years time, most new drugs will come under patent. When this happens, the system may be critical in determining whether or not countries can have access to generic medicines.” ■

Jacqui Wise, *Cape Town*

## Rich and poor countries divided on patent treaty

Developing countries fear that a proposed treaty to harmonize patent laws globally could have a devastating impact on their access to essential medicines, diagnostics and vaccines. A passionate and fractious debate around the proposed treaty underscores the vital role of trade and intellectual property for public health.

Indian HIV/AIDS activists and an international lawyers' group lodged an objection in late March 2006 to a patent application for an AIDS drug filed by a multinational company in India, arguing the patent would restrict access to this medicine. The case illustrates the impact that global harmonization of patent law could have on public health in developing countries, as it could remove the legal basis for such objections in future.

Last year, India, an important global provider of cheap generic medicines to other developing nations, adopted a new law on patents to bring the country in line with the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

Under the new law, the Indian Government retained the right of its people or companies to oppose new

applications for patents in India prior to approval by national patent offices. Now, groups fighting to improve access to medicines say proposals for global patent harmonization could strip national patent offices of this and other responsibilities.

The TRIPS Agreement established minimum standards for patents in WTO member states, but left room for each country to decide which patents to grant. In addition, TRIPS provided flexibilities, which were reinforced in the 2001 WTO Doha Ministerial Declaration, so that countries could escape some provisions in a public health emergency. Countries have barely used these flexibilities (see story on pp. 342–343) and now the work of another Geneva-based international body — the UN World Intellectual Property Organization (WIPO) threatens to eliminate them entirely.

Some TRIPS provisions were first

proposed when WIPO started working on global patent harmonization in the 1980s. In 2000, some procedures for patent filing worldwide were streamlined under the WIPO Patent Law Treaty. Since then, the European Union, Japan and the United States have pushed for further harmonization by reviving WIPO's efforts to harmonize substantive aspects of patent processing, i.e. aspects that go beyond procedure. But most of WIPO's 183 members stand firmly opposed to this.

The primary vehicle for harmonization at WIPO is the proposed Substantive Patent Law Treaty (SPLT), which is being negotiated by the WIPO Standing Committee on the Law of Patents. But since it was first proposed in 2001, the SPLT has snagged year after year, partly because its chief promoters, the European Union, Japan and the United States — the “trilateral” countries — cannot agree, but also because developing countries see little advantage in proceeding with it.

Developing countries fear that the proposed treaty would mean less autonomy in national decision-making with regard to patents, loss of TRIPS flexibilities, and higher prices for medicines.

“Quite clearly, it is not in the interests of developing countries to seek either a ‘light’ SPLT or a more comprehensive SPLT, since they have little to gain from a broader harmonization of substantive patent law,” said Professor Carlos Correa, Director of the Centre for Interdisciplinary Studies on Industrial Property and Economics Law at the University of Buenos Aires.

Correa and Sisule Musungu, Acting Coordinator of the Programme on Innovation, Access to Knowledge and Intellectual Property at the Geneva-based South Centre, argue that harmonization will lead to a situation where the United States’ definition of patent law is imposed on all countries. They have called for an assessment — governmental or independent — of the impact patent harmonization would have on developing countries.

Trilateral industry groups, meanwhile, are stepping up the pressure on WIPO to make progress towards harmonization. Phil Thorpe, Deputy Director of the United Kingdom Patent Office, warned that developing coun-

tries may lose influence in the debate if that debate moves outside WIPO, as some have suggested it should.

The trilateral proposal calls for discussions on four issues: the uses of a given innovation prior to patent application; possible patent protection when details about an invention have been disclosed before approval; how a product or an idea adds something new; and whether an innovation represents a step forward.

In addition, key developing countries have sought to include in these discussions talks on genetic resources, especially a requirement that the origin of the resources be disclosed in patent applications, and on protection of traditional knowledge (see story below).

The impact of the proposed treaty on patent harmonization will depend on how it defines what may or may not be patented, or patentability, according to Professor Brook K. Baker of the Northeastern University School of Law. Baker said that developed countries with strong innovative pharmaceutical industries have increased the scope of what can be patented, broadening the definition of, for example, what is new. This has led to a “growing insistence on patents for new uses, new formulations, new combinations, and for minor, therapeutically *de minimus* changes in chemical structures,” he said, referring to minimal changes that some argue should not be covered by separate patents at all.

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### Protecting traditional knowledge: the San and hoodia

The holders of traditional knowledge often face a dilemma. How can they benefit from their own traditional knowledge if they don’t patent it?

Intellectual property rights are often regarded as incompatible with traditional knowledge because patents are based on innovations or discoveries and held exclusively, while traditional knowledge is collectively owned and based on prior use.

In 2003, the San indigenous people (Bushmen) and South Africa’s state research institute the Council for Scientific and Industrial Research (CSIR) reached an agreement to share any royalties from potential sales of drugs or other products derived from the hoodia plant, *Hoodia gordonii*, which has long been known to the San as an appetite suppressor.

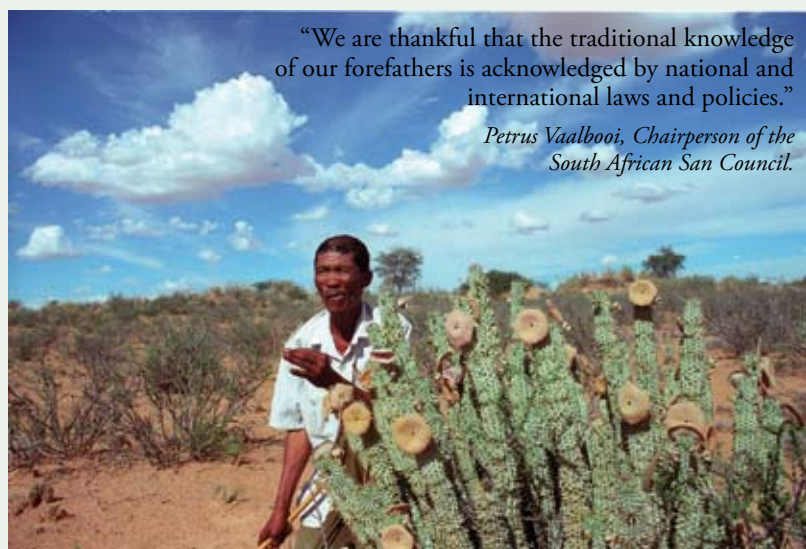
It was one of the first agreements to give the holders of traditional knowledge a share of the potential profits of products derived from that knowledge. A few years earlier the plant’s active ingredient had been patented by CSIR and licensed for further development to a British company which in turn sold additional licences to Pfizer and later to food multinational Unilever. The San also signed a profit-sharing agreement with the South African Hoodia Growers (Pty) Ltd in February 2006.

The appetite suppressant was to be commercialized into a food supplement and/

or prescription medicine, with considerable financial potential, but so far no products have been launched under the profit-sharing agreement. Recently lawyers representing the San filed complaints to the governments of Switzerland and Germany about hoodia products produced outside the agreement that were being sold in those countries. They said these sales were in contravention of international

agreements on biodiversity. In a letter sent in March 2006, they asked that the obligations of the Biodiversity Convention be honoured and that countries take steps to stop the sale of unauthorized hoodia products.

The San live in a region that cuts a swathe across Angola, Botswana, Namibia and South Africa. They are one of southern Africa’s most marginalized groups.



“We are thankful that the traditional knowledge of our forefathers is acknowledged by national and international laws and policies.”

*Petrus Vaalbooi, Chairperson of the South African San Council.*

Petrus Vaalbooi, Chairperson of the South African San Council, sampling a piece of a hoodia plant in the Brostdoring area in the San communal land of the Kalahari Desert in South Africa, 2004.

South Photographs/G. Williams

Baker said that new chemical entities represented the only area where harmonization of patentability could have a positive impact on access to medicines, but that the standards of patentability currently under discussion in treaty negotiations “would have a negative impact on public health, because they would expand the scope and extend the time period of patent protections on pharmaceutical products”. He added: “The predictable consequence is that prices will be higher and access lessened.”

The March 2006 objection to the Indian patent filing was that there was nothing new in GlaxoSmithKline’s fixed-dose combination of two existing HIV/AIDS drugs, zidovudine/lamivudine or AZT/3TC (Combivir), for which it was seeking a patent. Their argument: that the combination of two existing drugs — of which there are generic versions — is not an invention.

Ellen 't Hoen, Director of Policy and Advocacy at Médecins Sans Frontières, drew a link between the Indian case and the proposed treaty, as it shows the diversity in what may or may not be patented today. “If WIPO gets its way with harmonization there will be no diversity, meaning that a mistake in one patent office will not be corrected in another.”

She gave the example of the way strict patentability requirements in Indian law allowed the Indian Patent Office to reject a patent application from Novartis for the anti-cancer drug

Gleevec earlier this year, even though that patent had been granted in other countries. Following, opposition to the patent from a cancer patient association and generic companies, the Indian Patent Office rejected the application on the grounds that a new form of a known substance is not an invention.

But Louise Dunn, a spokesperson at GlaxoSmithKline, argued that the situation in India is evidence that patents are not a root cause for the lack of access to medicines.

“The root cause of developing countries’ inability to address their health-care problems does not lie with the patenting system but with a lack of funding, a lack of political will, and inadequate health-care infrastructure,” Dunn said, citing a common industry argument for inadequate access to medicines in developing countries.

The proposed treaty and its potential impact on public health remain highly controversial. A WIPO open forum on the proposed treaty in March 2006 showed that differences go deep and passions run high. Industry assertions similar to Dunn’s were vigorously opposed at the forum,

a meeting intended to feed the WIPO negotiating process.

Eric Noehrenberg, Director of International Trade and Market Policy at the International Federation of Pharmaceutical Manufacturers & Associations, told the WIPO forum that research and development-based industry is developing the best treatments for neglected

diseases, that patents are not blocking access to essential medicines in poor countries, that compulsory licences are harmful to countries, and that the debate over flexibilities in international agreements is an “industrial policy” debate not a health policy debate. He said industry had endeavoured to provide much-needed medicines to poor countries, but has

been blocked by the governments of those countries.

William Haddad, US generics industry leader and Chief Executive Officer of Biogenics, called Noehrenberg’s remarks “false and misleading”.

“These are real crises, not patent pricing arguments,” Haddad, a former US congressional aide, said: “We need real arguments”. ■

William New,<sup>a</sup> *Geneva*

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Ellen 't Hoen of Médecins Sans Frontières.

## Meeting the need for treatment: the initiatives

How do you stimulate research and development (R&D) for new drugs, vaccines and diagnostics, for which there will never be a lucrative market?

Many diseases prevail because drugs are old and ineffective, or simply do not exist. Tuberculosis (TB) is a major killer in poor countries, but no new anti-TB drug has been developed since the 1960s. There are rare, often life-threatening diseases, defined in Europe as affecting fewer than one in 2000 people, for which more “orphan drugs” need to be developed. There are diseases that are highly prevalent, such as HIV/AIDS in southern Africa, but

while new, effective medicines exist, millions of people and their governments cannot afford them or they are not available at all. Neglected tropical diseases, such as malaria, affect millions of people, but most are too poor to constitute a market that is lucrative enough to justify drug research and development (R&D) in industry terms.

Over the last decade, the world has recognized the problem and started to spend more on health research and

product development for these diseases. There has been a flurry of initiatives to address the lack of treatment for people in developing and developed countries. Many of these are outlined by WHO’s Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH), an independent panel of experts, in their final report: *Public Health, Innovation and Intellectual Property Rights* which was published on 3 April 2006 (see p. 351). For example, public-private partnerships have become a leading force in the development of drugs for neglected diseases; 46 such projects were in the pipeline in 2005, according to a Wellcome Trust report. The generic drugs industry provides cheap copies of brand-name

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medicines, has pushed down drug prices overall through competition.

Access-to-medicines campaigners and generic drugs companies argue that patents are a major barrier to meet the huge demand for affordable drugs, vaccines and diagnostics in developing countries.

In contrast, the R&D-based pharmaceuticals industry, which comes up with innovations and patents them to recoup the R&D costs, argues that the bottleneck is not the fault of patent restrictions, but the lack of funds to buy these products and inadequate infrastructure to deliver them.

## Generic industry

The global generic pharmaceuticals industry produces cheap copies of patented medicines for diseases such as HIV/AIDS, often pushing down the prices of the original patented medicines in the process. India is a major exporter of generic medicines to other developing countries. Of the more than 60 000 HIV/AIDS patients in nearly 30 countries in Médecins Sans Frontières' projects, 84% receive generic medicines made in India.

The generic industry helped establish the US Orphan Drug Act of 1983 to promote the development of medicines for small patient populations by providing incentives, such as tax benefits and exclusive marketing protection.

Some say this model could be used to promote the R&D for drugs for neglected diseases. The generic drugs industry sees several threats to its business model, such as "evergreening" by pharmaceutical companies to extend their patent rights and data exclusivity, i.e. denying the release of information required to advance science.

## Public-private partnerships

Public-private partnerships show that costly drug development can be combined with social responsibility.

Under a 2002 agreement with US pharmaceuticals company Chiron Corporation, the Global Alliance for TB Drug Development obtained exclusive world rights to the compound, PA-824, and its derivatives, which may be developed into a new TB medicine. Chiron agreed to make the compounds royalty free in endemic countries, while retaining the right to develop and commercialize them for non-TB indications.

Another example is a 2004 agreement between the International Partnership for Microbicides and Tibotec Pharmaceuticals, a Belgian subsidiary of pharmaceutical company Johnson & Johnson, to develop a microbicide to protect women from infection with HIV. Sanofi-Aventis is one of the partners of the Drugs for Neglected Diseases initiative's (DNDi) programme that has developed two combination medicines for malaria. This is a patent-free arrangement.

The Medicines for Malaria Venture is working on more than 15 anti-malarial projects with companies such as the Indian generics company Ranbaxy. The International AIDS Vaccine Initiative is developing vaccine candidates for people in developing countries. Its private sector partners include GSK (GlaxoSmithKline) Biologicals, Targeted Genetics Corp., Therion Biologics Corp. and Crucell.

## Patents

Some proponents of the patent system argue that it could be improved by raising the quality of patents and reducing the cost of using them. One proposal is to harmonize national and regional patent laws under the World Intellectual Property Organization's proposed Substantive Patent Law Treaty. Developed and developing countries are divided on this issue (see story on pp. 344–346).

There are two exceptions in the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) that have been made to allow governments to by-pass certain patent rights to address public health needs.

One is when a government issues a compulsory licence to allow a domestic manufacturer to use an invention without the patent holder's consent to produce a drug or vaccine for domestic consumption.

For example, local pharmaceutical companies may obtain compulsory licences to produce generic versions of patented or brand-name medicines. This has been extended to allow manufacture in another country, when the first country does not have a drugs manufacturing capability.

The second exception is parallel import. This is the import and resale in a country without the consent of the patent holder of a patented product that has been legitimately put on the market

of the exporting country. This means that drugs sold at a lower price in one country can be imported into another country where the same drug is sold at a higher price. Few governments have taken advantage of these two mechanisms, partly due to complex procedures (see story on pp. 342–344).

In its April 2006 report, the independent WHO Commission on Intellectual Property Rights, Innovation and Public Health made recommendations on how to improve access to drugs, vaccines and diagnostics in developing countries within the existing framework of international and national rules on intellectual property (see story on p. 351).

As a way to improve the patent system, the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) has proposed a "transferable market exclusivity" model under which a company would be granted patent extension for products, including blockbusters, that are marketed in developed countries, in exchange for doing R&D on neglected diseases for developing countries.

## Alternatives to patents

There are several proposals on how to provide R&D incentives to develop new drugs in the absence of patent protection.

A draft WHO Resolution (EB117.R13), sponsored by Brazil and Kenya, calls for additional R&D funding for new vaccines and medicines for diseases that mainly affect developing countries as part of a new global framework on essential health research and development. The proposal will be considered at the World Health Assembly on 22–27 May 2006.

The draft resolution draws on a 2002 proposal for a Medical Research and Development Treaty by non-governmental organization CPTech, which campaigns to improve access to medicines. The idea is that governments raise funds for R&D for neglected diseases by allocating a portion of gross domestic product (GDP) and other methods, and the government sets the R&D agenda.

Another proposal for raising R&D funding is the Medical Innovation Prize which has been put forward in a bill in the US Congress. Under the proposed legislation, new drugs would be treated as generics as soon

as they receive regulatory approval and patent holders would be rewarded from a US\$ 60-billion award fund for coming up with innovations for better health. The fund would receive 0.5% of US GDP every year.

The Group of Eight (G8) industrialized countries is exploring the advance market commitment (AMC) proposal. Under this scheme, sponsors or donors would make legally binding financial commitments to buy vaccines before they are developed, and companies would supply a successful vaccine at a pre-guaranteed price.

The aim would be to encourage more research into and development of vaccines for neglected diseases in developing countries. It is unclear, however, whether advance purchase can spur research into second- and third-generation vaccines, and how to set a price before a vaccine has been invented.

Open access publication of scientific findings is another initiative to encourage the sharing of scientific research findings as widely and rapidly as possible. For example, the Wellcome Trust, the largest nongovernmental source of funds for biomedical research in the United Kingdom, mandates that all the research it funds is published in open-access journals or other fora.

Researchers at the US National

Institutes of Health, one of the world's leading research centres, are also encouraged to publish their findings in open-access fora (see pp. 339).

### Patent donation and pooling

Pharmaceutical companies often donate medicines but patent donation is more common in the software industry. For example:

The University of California, Santa Barbara (UCSB), donated a patent that covers the novel use of an established class of cardiovascular medicines, calcium channel blockers, as a potential new drug against the parasitic disease, schistosomiasis, to non-profit pharmaceutical company, the Institute for OneWorld Health, in February 2004.

The University of Nebraska has assigned the Medicines for Malaria Venture the rights to the patent applications and patents on synthetic peroxide technologies to develop medicines for malaria, with no licences involved or payment to the university.

Colombian scientist Manuel Patarroyo donated the patent for a potential malaria vaccine to WHO in 1995, but clinical trials have proved disappointing.

Patent pooling is an agreement between two or more patent owners to license one or more of their patents

to one another or to third parties. CoroNovative, a for-profit spin-off of Erasmus University, proposed patent pooling with other researchers to sequence the gene for SARS (severe acute respiratory syndrome), to prevent a fragmentation of research that would hinder vaccine development.

### Philanthropy

Charitable organizations, often private and corporate philanthropic foundations, donate money to drug development projects. There is a long history of philanthropy for drug development. An early project of the Rockefeller Foundation was to fund development of a yellow fever vaccine. There are many others: the Bill and Melinda Gates Foundation, the Kaiser Family Foundation, in the United Kingdom, there is the Wellcome Trust and in India the Tata Memorial Centre.

There are pharmaceutical industry examples as well. The Novartis Institute for Tropical Diseases in Singapore focuses on dengue fever and tuberculosis. US companies, Pfizer, Merck and Johnson & Johnson as well as GlaxoSmithKline of the United Kingdom and Germany's Bayer have also donated medicines and funds for medicines for developing countries or towards R&D for diseases that affect those countries most.

### Government tax initiatives

The United States introduced the Orphan Drug Act in 1983 to promote the development of medicines to treat diseases that affect less than 200 000 people in the country. Under that law, companies are offered various incentives to develop and manufacture drugs that would otherwise not be regarded as profitable.

The United Kingdom offers enhanced tax relief for R&D into vaccines or medicines for diseases that mainly affect developing countries, such as malaria, tuberculosis and HIV/AIDS. Vaccines Research Relief is an initiative of the UK Department (ministry) of Trade and Industry. Another UK proposal is that a government authority could procure R&D efforts through measures such as contract grants, and the innovations would be used by the procurer or be placed in the public domain. ■

Tove Iren S. Gerhardsen,<sup>a</sup> *Geneva*



WHO Digital Photo Library

New medicines have transformed the lives of people across the world. With the advent of powerful new anti-tuberculosis drugs in the 1960s, families such as this one in the Indian city of Chennai could be cured at home. Since then, however, no new drugs for the disease have been developed despite growing drug resistance and increasing incidence of tuberculosis in places where the prevalence of HIV/AIDS is high.

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