

HIV/AIDS

Antiretroviral

Newsletter - UPDATE



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The aim of this newsletter is to provide health workers in the Region with a brief, up-to-date summary of the latest developments in antiretroviral therapies.

TRIPS, INTELLECTUAL PROPERTY RIGHTS AND ACCESS TO MEDICINES¹

THE TRIPS AGREEMENT

The Agreement on Trade-related Aspects of Intellectual Property Rights (or the TRIPS Agreement) is an integral part of the World Trade Organization (WTO) Agreements, which create binding international obligations among WTO Member States. The TRIPS Agreement is subject to the WTO's dispute settlement mechanism, which may -as a last resort- allow Member Countries to apply trade sanctions against a non-compliant Country, thereby ensuring enforcement of the WTO's rules and agreements.

TRIPS AND PATENTS

Patents are a public policy tool; they were designed to promote and reward innovation, while at the same time ensuring disclosure of the invention, in order to make it widely known and available. Before TRIPS, countries could -and did- devise a patent regime that was in line with their level of development and their overall, national priorities.

The TRIPS Agreement has to a large extent harmonised the standards for patents; notably, it makes it mandatory for countries to ensure that patent protection is available in all fields of technology, for both process and product inventions. Thus, it is no longer possible for countries to exempt pharmaceuticals from patent protection (as a number of countries did, before TRIPS came into force). Nor can countries like India continue to limit pharmaceutical patents to process patents only.

The distinction between product and process patents is important, since if a product is patented, only the patent holder may make or sell that product; nobody else may do so, unless the patent holder has given permission (a license). In the case of a process patent, nobody may make that product *by using the process that is protected*.

¹ This ARV newsletter has been updated in January 2006.

However, if someone can produce the same product in a different way, he/she may do so. Since for most pharmaceuticals multiple routes of synthesis can be devised, process patents offer considerably less protection than product patents². Until 2004, India recognized only process patents for drugs. Thus, India implicitly provided incentives for local manufacturers to "invent around" the patent (i.e. to develop a different production method); generics thus produced were legal in India, and, as a result, generic versions of newly developed drugs used to be available relatively quickly in India. This will change, because from 2005 onwards India will implement TRIPS (see also below).

TRIPS furthermore requires that the minimum duration of patent protection is 20 years (prior to TRIPS, the patent term was 20 years in certain industrialized countries, but shorter in many developing countries), and mandates effective enforcement.

The introduction of these TRIPS standards will delay the marketing of generic versions of new drugs, and, thus, the competition they entail; hence it is anticipated that prices of new drugs will remain high for a longer time³ which will result in reduced access for many people, notably in developing countries.

ACCESS TO DRUGS

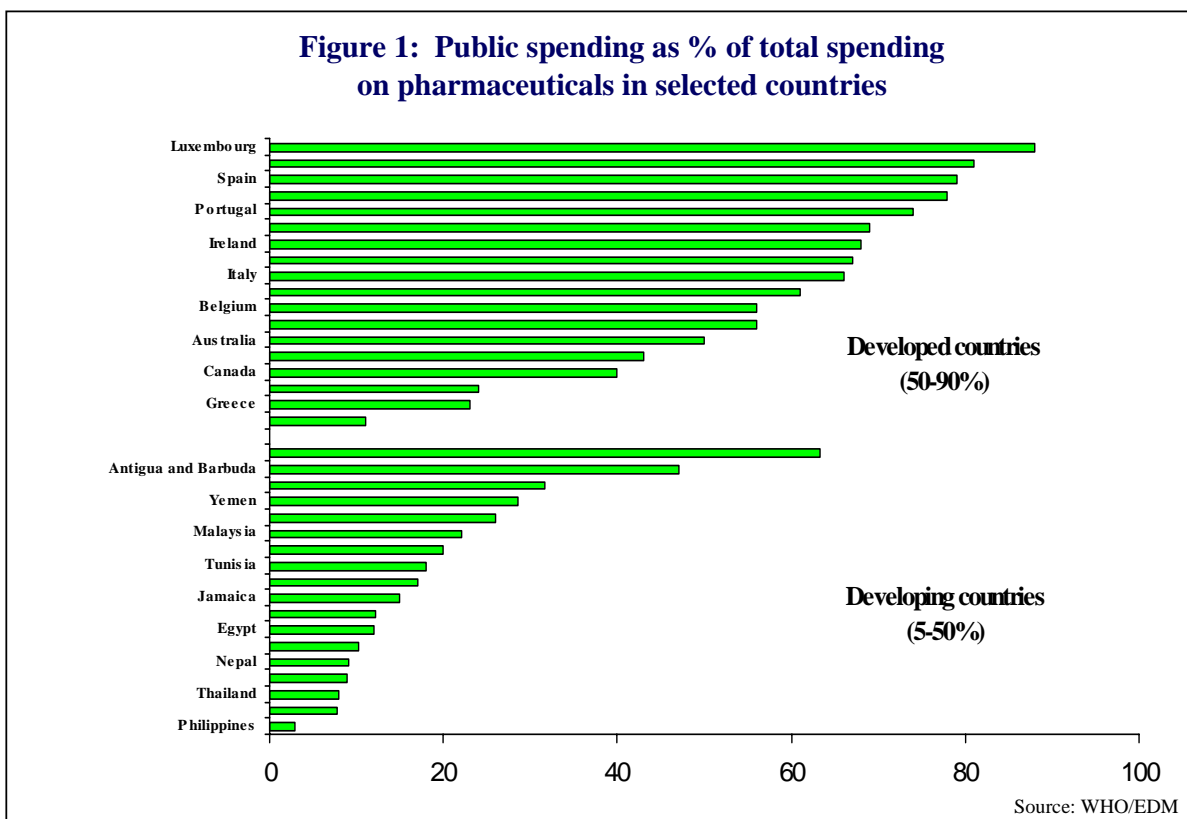
Access to medicines depends on many factors, notably rational selection and use of drugs, adequate and sustainable financing, affordable prices, and reliable supply systems. Prices are only one factor⁴. Yet prices are an important factor, especially in developing countries, since, while in developed countries pharmaceuticals are largely publicly funded, through reimbursement and insurance schemes, in developing countries, typically, 50-95% of drugs are paid by the patients themselves (see Figure 1). Thus, in developing countries, prices have direct implications for access to medicines.

² TRIPS has however reinforced process patents.

³ TRIPS does not apply retroactively, therefore there are no implications for drugs that were already off-patent when TRIPS came into force.

⁴ It should also be noted that patents are not the only reason for high drug prices; distribution costs, high mark-ups and taxes can also play an important role.

Figure 1: Public spending as % of total spending on pharmaceuticals in selected countries



TRIPS SAFEGUARDS

It is however important to realize that TRIPS is a framework agreement; it is to be operationalized via countries' national laws. Moreover, TRIPS does contain -limited- flexibility, as well as some safeguards, which can be used to mitigate the anticipated negative impact on drug prices and on access to drugs.

The most important safeguards are (i) compulsory licensing, (ii) parallel importation and (iii) provisions for early working (often referred to as "Bolar provision").

The "Bolar provision" allows testing and regulatory approval of generic versions of a drug, *before* its patent expires; thus, it allows generic producers to get ready, so that they can start the production and sale of a generic drug as soon as its patent expires⁵. In this way, a Bolar provision facilitates generic competition.

Parallel importation refers to importation, without the consent of the patent holder, of a patented product that is marketed in another country. Parallel importation allows one to 'shop around' for a good price; for example, if a company sells drug X in country A at a price of \$10, while the same company sells the same drug X in country B for \$1, then someone may import drug X from country B and sell it in country A, charging for example

⁵ In the absence of such a provision, generic manufacturers can only start the time consuming process of testing and registration after the expiry of the patent; this can easily delay the marketing of generic drugs to 2-3 years after patent expiry.

\$3. As a result, in this example, country A would save \$7 on product X. In other words, parallel importation also enables competition, but in a different way.

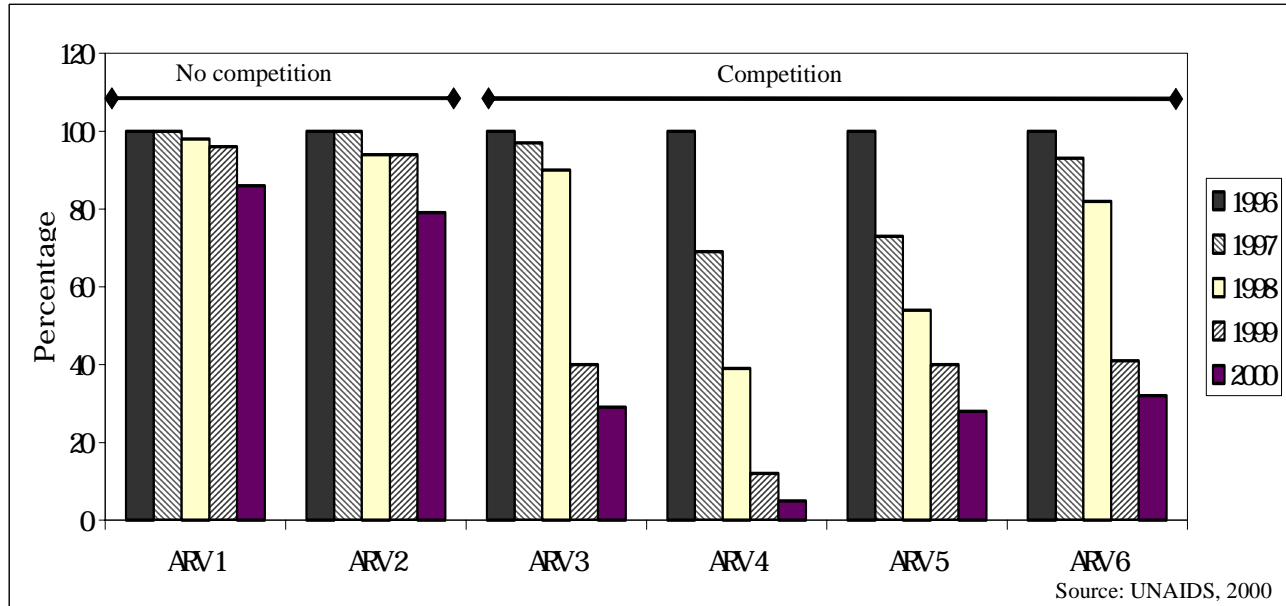
The TRIPS Agreement states that parallel importation cannot be challenged under the WTO dispute settlement mechanism, thus de facto leaving countries the freedom to choose whether or not to allow parallel importation. Moreover, during the WTO's Ministerial Meeting in November 2001, the Ministers clarified, in the Doha Declaration on the TRIPS Agreement and Public Health, that countries are free to use parallel importation.

A *compulsory license* is a license to use an invention, which has been granted without the permission of the patent holder. A compulsory license can be used to allow the production and sale of generics before expiry of the patent - thus, again, increasing opportunities for competition (and competition drives prices down, as can be seen in Figure 2).

The basic rationale for a compulsory license is that, since a patent is a privilege granted by the government, the government retains the right to limit that privilege if necessary. Many countries, including many developed countries, have provisions for compulsory licenses in their national laws, and compulsory licenses are allowed under TRIPS.

TRIPS mentions that a compulsory license can be issued for reasons of national emergency or extreme urgency, public non-commercial use and other reasons. However, it is important to note that TRIPS does *not* limit the grounds, or reasons, for issuing a compulsory license.

Figure 2: Influence of competition on drug prices
1996 prices taken as reference (100%)



But the TRIPS Agreement does specify *conditions*, which are to be imposed by governments when issuing a compulsory license. These conditions include⁶:

- case-by-case decision
- first try to obtain a voluntary license
- adequate remuneration to the patent holder
- predominantly for the supply of the domestic market
- a compulsory license should be non-exclusive and non-assignable.

So while these conditions have made the process somewhat cumbersome, it is possible to issue a compulsory license in a TRIPS-compliant way.

A special case of compulsory licensing is ‘*Government use*’ (or a compulsory license for public non-commercial use). TRIPS imposes less stringent conditions in case of ‘*Government use*’; hence countries may find that using this mechanism is easier/faster than compulsory licensing.

However, the safeguards provided for in TRIPS can only be used when incorporated in the national law. Thus, it is important that countries design and enact legislation which allows them to protect the public interest, including the public health interest.

⁶ The list is not exhaustive; moreover, certain conditions may be waived in specific circumstances. For instance, the condition to first try to obtain a voluntary license does not apply if a compulsory license is issued to remedy anti-competitive behavior of the patent holder, in case of an emergency or in case of public non-commercial use.

FLEXIBILITY IN TRIPS

In addition, as mentioned above, there is some flexibility in TRIPS. For example, one of the conditions for issuing a compulsory license is that the patent holder should receive adequate remuneration. But TRIPS does not define “adequate”; thus, countries have some leeway in this respect.

Similarly, TRIPS leaves countries free to use either very strict or more flexible criteria for patentability. Applying flexible criteria of novelty and inventiveness enables for instance the issuing of patents for formulations or for isomers of known drugs, thus allowing pharmaceutical companies to apply for additional patents, and providing them with opportunities to expand the duration of protection beyond that of the original patent. In this way, originator companies can seek to postpone generic competition.

Yet whether this flexibility is actually used in order to facilitate access to medicines ultimately depends on national standards and (administrative) procedures.

OTHER TRIPS PROVISIONS

Patents are not the only type of intellectual property rights addressed in TRIPS, and some of the other forms of intellectual property can also have implications for access to drugs. For example, TRIPS mandates protection of undisclosed data submitted to national Drug Regulatory Authorities in order to obtain marketing authorization for new drugs. These registration data have to be protected against disclosure, and against unfair commercial use. Thus, the national

authorities may not publish such data or share them with competing (e.g. generic) companies.

Some parties however try to argue for *data exclusivity*, which means that the regulatory authorities would not be allowed to rely on these data for the purpose of registration of generic versions of the drug. By implication, as long as the exclusivity lasts, generic producers would either have to submit their own data - which would oblige them to repeat the clinical trials and other tests- or they would have to delay the launch of their product until the end of the exclusivity period. Thus, data exclusivity diminishes the likelihood of speedy marketing of generics, and delays competition and price reductions.

TRIPS, however, mandates data protection, but not data exclusivity and national laws need not have requirements that are more stringent than TRIPS⁷.

Similarly, it is important that national trademark laws do *not* hinder pro-public health measures such as generic prescription, generic substitution and/or requirements that a drug's label includes the generic name.

COUNTRY EXPERIENCES

Two countries that are at the forefront of the fight against HIV/AIDS, especially with regard to making HIV/AIDS drugs, including antiretrovirals (ARVs), available and affordable, are Thailand and Brazil. Thailand focuses on producing and selling generic ARVs at the lowest possible price⁸, while Brazil is providing free ARV treatment in its public health facilities. Their strategies, with regard to intellectual property rights, are summarized below:

THAILAND

The Government Pharmaceutical Organization (GPO) in Thailand is producing a number of generic ARVs. The GPO is only producing products that are not patented in Thailand, or for which the Thai patent has expired. One important drug, didanosine or ddI, used to be under patent in Thailand; however, the patent only applied to ddI tablets. Hence the GPO has been producing ddI powder; the powder form, while not as convenient or as accurate a dosage form as tablets, did not infringe the patent.

Some years later, following a challenge by NGOs representing people living with HIV/AIDS, Thailand's Central Intellectual Property and International Trade Court has ruled that the ddI patent was only valid for tablets containing 5-100 mg ddI. Since then, it has been possible for generic producers, such as the GPO, to

⁷ Unfortunately, data exclusivity and other requirements that go beyond TRIPS are increasingly being incorporated in bilateral/regional free trade agreements.

⁸ The Thai Ministry of Public Health also provides highly subsidized ARV treatment via its universal coverage scheme (the '30 Baht scheme').

⁹ The first generation of ARVs that were patented in the 1980s will continue to come off patent.

produce ddI tablets outside that dosage range (e.g. tablets containing 125 mg ddI).

BRAZIL

Brazil, like Thailand, has a government-owned company that produces generic versions of certain ARVs, which are not under patent in Brazil. In addition, Brazil has used the fact that it is capable of producing generic versions of crucial HIV drugs, and that it would be willing to issue a compulsory license if necessary, to negotiate substantial price discounts for those drugs that are patented. So far, this strategy has been quite successful, and Brazil has not yet had to actually issue a compulsory license.

MALAYSIA AND INDONESIA

Increasingly, other countries are also taking action in order to make ARVs more available and affordable. In Oct. 2003, Malaysia decided to apply 'Government use' provisions in its national law in order to import generic ARVs. A year later, Indonesia used the 'Government use' mechanism for domestic production of several generic ARVs.

OPTIONS FOR OTHERS

So what can other countries do? What options are available to increase access to HIV/AIDS drugs? Clearly, the answer will vary considerably from country to country, depending on relevant national laws, production capacity and other factors. But in principle, the following options exist:

Countries with pharmaceutical production capability could initiate local production of generic versions of those drugs that are not patented or whose patents have expired⁹. They could also consider, *if their national law and regulations allow*, to apply compulsory licensing or 'Government use' to enable local production of generic versions of those drugs that are patent protected.

Countries where local production is not feasible or not viable can import generics, for example from India, provided the drug concerned is not under patent in their territory. In case the drug of interest is patent protected in the importing country, parallel importation could be considered, as long as national legislation allows it - and if a cheaper source of the drug can be found.

The option to (parallel) import obviously is also open to countries that do have manufacturing facilities. Yet a problem looms: major international producers of generics are primarily located in countries such as India, which now have to comply with TRIPS (see Figure 3; India falls in category c). Fortunately, transitional provisions in India's new patent law allow the continued production of generic medicines marketed before 2005. However, Indian pharmaceutical enterprises will have to wait until patent expiry before they can commence the production of *new* generics. Thus, even when patents in their own territory do not stand in the way, importing countries may face problems in finding a source of supply of generic versions of second line ARVs and other new drugs.

Meanwhile, countries that lack national production capacity would face difficulties in making effective use of compulsory licensing provisions. The basic problem is that while the importing country could use compulsory licensing or 'Government use' for importation of the drug from abroad¹⁰, foreign companies would -because of TRIPS' condition that a compulsory license should be issued "predominantly for the supply of the domestic market"- face potentially severe restrictions on their capacity to export.

During the WTO meeting in Doha, Ministers recognized this problem, and instructed the WTO's TRIPS Council to find an expeditious solution. But because of

diverging views there has been considerable debate on how to best tackle this inconsistency.

A solution was finally agreed to on 30 August 2003. This solution, which may require two compulsory licenses to be issued (one in the importing and one in the exporting country)¹¹ and has been criticized as being cumbersome, has not yet been used in practice. This may, among other reasons, be due to the fact that most exporting countries would have to amend their national laws before they can actually export generic medicines produced under a compulsory license – something that Canada, Norway, India, South Korea and China have recently done.

Figure 3: Deadlines for implementation of the TRIPS Agreement	
a) Developed countries	1996
b) Developing countries (except those under c)	2000
c) Developing countries that did not grant pharmaceutical product patents prior to TRIPS	2005
d) Least developed countries	2016*

** The original TRIPS implementation deadline for least-developed countries was 2006; however during the WTO Ministerial Meeting in Doha, it has been agreed to extend this deadline.*

FURTHER READING

1. Globalization and Access to Drugs: Perspectives on the WTO/TRIPS Agreement – WHO, Geneva, 1998.
2. The TRIPS Agreement and Pharmaceuticals – (ASEAN workshop report) MOH/WHO, Indonesia, 2000.
3. Integrating Public Health Concerns into Patent Legislation in Developing Countries – South Centre, Geneva, 2000.
4. Manual on Good Practices in Public-Health-Sensitive Policy Measures and Patent Law – Third World Network, 2003.
5. Implications of the Doha Declaration on the TRIPS Agreement and Public Health – WHO, Geneva, 2002.
6. Protection of Data Submitted for the Registration of Pharmaceuticals – South Centre/WHO, Geneva, 2002.
7. Implementation of the WTO General Council Decision on Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health – WHO, Geneva, 2004.

Documents 1, 2, 5 and 7 (as well as other relevant materials) can be downloaded from: <http://www.who.int/medicines/>

Documents 3 and 6 can be found at: <http://www.southcentre.org/>

ACKNOWLEDGEMENTS

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¹⁰ Using a compulsory license for importation appears to be permissible under TRIPS.

¹¹ In addition, there are requirements to report to the WTO and on labelling/packaging of the concerned medicines.