

Questions on Intellectual Property and Access to Drugs for HIV/AIDS

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Q1. How many people suffer from AIDS?

A1. According to the most recent (2004) UNAIDS estimate, about 39.4 million people worldwide are living with HIV/AIDS. Of the total, about 36.58 million live in developing countries, including 25.4 million in sub-Saharan Africa. Last year, UNAIDS estimates 3.1 million people died, primarily in developing countries.

Q2. Are there patents on AIDS drugs in developing countries?

A2. Yes, but the situation varies from country to country, and from drug to drug.

Some products are rarely patented in poor countries at all. Stavudine, an AIDS drug discovered at Yale University, is only patented in 1 African country (South Africa) where it is still available as a generic, because Yale declines to enforce its patent there. On the other hand, the patent is enforced in other developing countries, such as Mexico, Romania and the Philippines.

Other drugs are more widely patented. 3TC and combivir – two key drugs for low priced HAART regimes – are patented in 33 and 37 African countries¹, respectively, and widely patented in other developing countries. Nevirapine, another important drug is patented in 25 African countries. Drug patents in Africa often cover the drugs most appropriate for treatment in Africa, given their cost of production and ease of administration. They also tend to be found where the general population and HIV prevalence is highest, and in countries with above average wealth.

Q3. Do patents represent a real barrier to access?

A3. Yes. Patents grant producers monopoly power, and prices are set to maximize profit – higher than the marginal cost of production, and significantly higher than the price that would exist in a competitive market. Currently, many treatment programs in Africa are ignoring WTO patent rules by purchasing generics without issuing compulsory licenses. This is unsustainable, not only because it violates the TRIPS Agreement, but also because it violates donors' funding guidelines.

Q4. Haven't the patent holders lowered the prices of their antiretrovirals?

¹ Amir Attaran and Lee Gillspie-White. "Do Patents for Antiretroviral drugs Constrain Access to AIDS Treatment in Africa?" *Journal of the American Medical Association*. October 17, 2001 – vol 286, no. 15

A4. Yes, but generics are still less expensive. At first patented drugs were priced up to 99 times higher than their generic counterparts. Under the sustained threat of generic competition they agreed to a series of price cuts. Despite many claims of pricing at "no profit" generic drugs are still priced lower in most cases. Generic prices on the most heavily used antiretrovirals that make up the backbone of first-line HAART therapy are still lower.

The brand-name drugs which have had their prices reduced tend to be the drugs which people beginning antiretroviral therapy are first prescribed. As people remain on antiretroviral therapy, they develop resistance and need to switch to different drugs. Medicines used in these "second-line" treatments are far more expensive. For example, Boehringer-Ingelheim sells nevirapine in poor countries for \$438 per patient per year, but Roche sells saquinavir in poor countries for up to \$2362 per patient per year.²

One of the main determinants of the price of a drug is whether there is a large enough market for its Active Pharmaceutical Ingredient (API). Due to the large size of Brazil's AIDS treatment program, the APIs for the drugs produced for Brazil's program have competitive markets and therefore considerably lower costs-per-kilogram. According to WHO's recent 3x5 Report, the upper-bound costs-per-kilogram for the APIs used in both AZT and 3TC – two older drugs which have been mass-produced in Brazil for years – is near \$500. On the other hand, APIs for newer drugs not mass produced in Brazil can cost thousands of dollars per kilogram (\$3500 for Abacavir; \$4000 for Lopinavir).

Q5. Are generic drugs safe and effective?

A5. There are many producers of generic drugs, and there are legitimate quality concerns with some of them. In order to be sure a generic drug is safe and effective, the purchaser should be sure that it has been approved by a reliable national regulatory authority – such as the USFDA or its counterparts in Thailand and South Africa – or prequalified by the World Health Organization.

To gain marketing approval from a national regulatory authority, a generic producer must show that its product is bioequivalent to the branded version of the medicine. Bioequivalence means that the generic drug releases the same active ingredient into the body at the same rate. The World Health Organization also inspects the manufacturing processes and quality of HIV-related medicines - both branded drugs and generic. The ones that pass a rigorous inspection process (much like that used by the FDA or other national regulatory authorities) are then "prequalified" by the WHO.

Q5a. Critics of the WHO prequalification process have insisted that it is not a replacement for FDA approval. Are WHO prequalified drugs safe?

² Médecins sans Frontières. "Untangling the Web of Price Reductions." 7th edition. February, 2005.

The WHO prequalification process involves inspections akin to those required by the best national regulatory authorities. Companies must have both their test data and their physical facilities inspected.

Q5b. Doesn't the recent delisting of some Indian generic drugs from the WHO prequalification list indicate problems with the quality of generic drugs tested by WHO?

No. While WHO recently removed six antiretrovirals produced by Cipla and Ranbaxy from its list of prequalified drugs, this is not a sign that WHO prequalification system is flawed. The delisting was due to an audit of an independent Contract Research Organization (CRO) hired by the drug companies to conduct bioequivalence studies that showed the CROs were not in compliance with good clinical and laboratory practices. The drug companies suspended business with this CRO and began retesting their drugs. Last November, some of Cipla's antiretrovirals were put back on the prequalification list.

While some have used this fact to attack the credibility of the prequalification system, the fact is that it proves there are rigorous standards and effective monitoring of the drugs. The WHO prequalification system is not the only standard bearer to remove drugs from the market – the USFDA removed the high-profile drugs Vioxx and Paxil from the US market due to serious side effects. Actually, the USFDA finds and reports hundreds of violations every year, sometimes leading to the removal of drugs from the market, sometimes not. No regulatory system is perfect and problems with products will always arise. When this happens, removing drugs from the market is what regulators are *supposed to do*.

Q6. Is antiretroviral therapy feasible in resource-poor settings? Won't there be problems with adherence?

A6. Antiretroviral therapy is indeed feasible and happening right now in resource-poor settings. Health workers on the ground in some developing nations report adherence levels that equal or exceed those in American cities. However, in order to have sustainable distribution of AIDS treatment, infrastructure must be built up, and a reliable supply of low-cost medicines must be put in place.

Resistance is a problem in rich countries and poor countries alike. Many people with HIV/AIDS in the US have been on HAART for years and have built up resistance to numerous drug regimens. This is not offered by anyone as a reason to deny treatment to Americans. As the worldwide number of people on HAART rises, prices on second-line antiretrovirals will become more of an issue, and further competition from generics will be needed to drive prices lower.

Q7. Will the US government buy generic versions of patented antiretrovirals in its AIDS programs abroad?

A7. Yes, although it has been slow to actually begin purchasing them.

The US government's biggest program to fight AIDS abroad is known as the President's Emergency Plan for AIDS Relief (PEPFAR). This program funds antiretroviral treatment, palliative care, prevention programs, and care for orphans in 15 countries.

PEPFAR's procurement policy is to purchase only drugs that have received marketing approval from the FDA. (It will not accept WHO prequalification or another nations' regulatory approval as an assurance of quality.) The FDA has set up a system of "rapid review" for generic firms seeking to sell generic antiretrovirals to PEPFAR, but only one cocktail by one firm has been approved. Critics of PEPFAR assert that preparing bioequivalence studies for the "rapid review" is extremely costly and time consuming, as well as unnecessarily duplicative (since tests have already been conducted for the WHO prequalification listing).

Q8. Do WTO intellectual property rules (the TRIPS Agreement) prevent Members from buying generic versions of patented antiretrovirals?

A8. All WTO Members can purchase and use generic versions of patented medicines by issuing compulsory licenses for the patents to third parties. (WTO Members that are designated by the World Bank as Least Developed Countries do not have to issue pharmaceutical patents until 2016.) The WTO's TRIPS Agreement specifically permits compulsory licensing, though certain conditions must be met, including payments of royalties to the patent owners. Malaysia, Indonesia, Zambia, Zimbabwe, South Africa and Mozambique are among the countries that have recently taken advantage of the TRIPS flexibilities for issuing compulsory licenses.

Q9. Can a country that doesn't have a reliable, efficient pharmaceutical industry import patented drugs from another country?

A9. The TRIPS Agreement places no restrictions on importing compulsorily licensed goods. In cases where there is no patent in the exporting country, any WTO Member can import generic versions of a drug for which it has issued a compulsory license. Problems arise on the exporter side when a country intends to import a generic drug that is under patent in the exporting country, because Article 31.f of the TRIPS Agreement states that compulsory licenses should be issued "predominantly for the supply of the domestic market." (This is waived under Article 31.k, which covers compulsory licenses issued to remedy anticompetitive behavior.)

WTO Members realized Article 31.f could pose a problem for countries which didn't have a domestic industry capable of efficient pharmaceutical production. In the 2001 Doha Declaration on the TRIPS Agreement and Public Health, they agreed to address this problem. Before the 2003 Ministerial in Cancun, the WTO issued a Decision clarifying that those countries with "insufficient or no manufacturing capabilities in the pharmaceutical sector" could indeed import drugs from other countries. The Decision imposes a number of conditions on these interactions, including notification by the importing Member that it intends to use the system and that it lacks production capacity,

and has taken measures to prevent the diversion of low-priced generics into rich-country markets.

Canada, Norway, and India have passed legislation that will allow its drug producers to take advantage of this WTO Decision. While implementing regulations are still under consideration in both Canada and Norway, pharmaceuticals are already available and in widespread use from Indian firms. Similar legislation is under debate in the Netherlands, Switzerland, Korea, and the European Community.

Q11. India supplies many generic AIDS drugs to developing countries. Recently the Indian Parliament passed new legislation to amend the patent law in order to comply with the TRIPS Agreement, and concerns have been raised that the legislation contains many TRIPS-plus barriers to access to medicines. How will the law affect the worldwide supply of generic medicines?

A11. India had until 2005 bring its patent law into compliance with the TRIPS Agreement, but it did not meet the deadline. A very restrictive presidential Ordinance went into effect in December 2004 while the Parliament continued to debate the Amendments to the Patents Act. At first, the legislation was very similar to the Ordinance, but the Parliament made certain revisions before passing the bill.

The new legislation allows export to countries that have followed WTO procedures, whether or not this includes the issuance of a compulsory license.

There was also concern that the Indian legislation would restrict the export of generics patented in India but produced there under compulsory license. The new legislation states that in this case “the license is granted with a predominant purpose of supply in the domestic market, and that the licensee may also export the patented product, if need be in accordance with Section 84(7)(a)(iii).” However, no generic firm can receive a patent until three years after a product has been on the market, and critics of the legislation fear that the process for obtaining a license is overly legalistic and cumbersome – giving patent owners many opportunities to fight licenses in the courts, and acting as a disincentive to generic firms to seek compulsory licenses in the first place.

The patent law also includes a “mailbox” provision. Companies have been filing patent applications for drugs discovered since 1995. This year the patent office will begin examining these applications, and any patent granted will be effective for 20 years from the date of application. Many thousands of patents – many of low quality – have been filed. The new legislation includes the mandatory issuance of compulsory licenses to generic producers that have already been producing a drug if and when that drug receives a patent through the mailbox provisions. Generic producers will not be forced to halt production, but under WTO rules, they will have to pay royalties to the patent owners.

Q12. What is the World Health Organization's "3 by 5" program?

A12. "3 by 5" is the World Health Organization's goal to have 3 million people on antiretroviral treatment by the end of 2005. (This is half the estimated 6 million people that WHO estimates are in immediate need of antiretroviral therapy.) 700,000 people were on HAART by the end of 2004. In order to fulfill its goal, 2.3 million more must begin antiretroviral therapy by the end of the year.

Q13. If countries buy low-priced generic drugs instead of purchasing drugs from brand-named pharmaceutical firms, how can the industry continue to invest heavily in R&D? Won't this reduce the number and quality of future innovative treatments?

A13. Marketing drugs at extremely high prices in countries where most people could never afford them was not a lucrative model to begin with, and now a number of companies have lowered their prices to what they claim are "no profit" levels. Rich countries account for the vast majority of pharmaceutical industry sales.

Paying high prices for pharmaceuticals is one way to fund medical innovation, but it is not necessarily the best way. IRS data shows that 13% of industry sales were re-invested into research and development. According to the FDA, 70% of the medicines approved for marketing in the US provide "little or no" improvement over existing therapies. So a fraction of a fraction of the money sent to branded pharmaceutical companies is invested in important research.

Public Health groups are advocating an R&D Treaty where countries would agree to invest a certain percentage of their GDP on medical research, and in return would agree not to use TRIPS or other FTA enforcement mechanisms against each other with respect to drug patents. Signatories would be free to fund R&D however they wanted, through paying high prices, direct government funding of research, prize models, competitive intermediary funding sources, or any other system they chose.

For more information, see the Consumer Project on Technology's website on intellectual property rights and healthcare, online at www.cptech.org/ip/health