

PHARMACEUTICAL ACCESS AND RESEARCH INCENTIVES: STAYING TRUE TO TRIPS?

In searching for a solution to the continued struggle over TRIPs and the Doha Declaration, two problems need to be solved: first, how to provide poor countries with an adequate supply of current drugs, and second, how to ensure that new drugs are developed for the treatment of “neglected” tropical diseases that lack effective low-cost drug therapies. These include malaria, tuberculosis, sleeping sickness, Chagas disease, and leishmaniasis. There are two opposing perspectives on these two issues: the solutions proffered by the pharmaceutical industry and the approach taken by NGOs, such as Health Action International, Médecins Sans Frontières, Consumer Project on Technology and Oxfam. In resolving these issues, international organisations such as the WHO have become central.

■ Access to current drugs

Access to current drug therapies in developing countries depends on an adequate health infrastructure for delivering drugs and the cost of these drugs. Both NGOs and the industry agree on these two requirements, but they take different positions on their relative importance. The industry has argued, in respect to HIV/AIDS drugs in Sub-Saharan Africa, that prices and patents are not the problem. The IFPMA has stated that even free drugs would not go very far in solving the problem of HIV/AIDS due to poor health infrastructure. Similarly, the Pharmaceutical Research and Manufacturers of America (PhRMA) stressed that the “real barriers to access to medicines in developing countries” is not TRIPs but “poverty, too few trained doctors and adequately equipped facilities, high tariffs on medicines in many developing countries, the need for more developed country support, and political will in developing and developed countries alike”.¹

Clearly it is necessary to improve the health infrastructure in developing countries. Although largely a task for governments and international organisations, several pharmaceutical companies, such as Merck, Pfizer, and Bristol Myers Squibb, support HIV/AIDS education and clinics as part of their philanthropy programmes. These programs can also benefit the donors by developing an infrastructure for clinical trials of new drugs and vaccines.

Even where health care systems are adequate, affordable prices and the supply of drugs to meet the needs of developing countries remain at issue. Industry opposes the two methods to deal with these problems provided by TRIPs for national emergencies and which the Doha Declaration reconfirms: parallel imports and compulsory licensing. Either or both methods can be used by governments to lower drug costs and widen the supplier range. The industry argument against these two methods is that they will reduce the profit incentive for research into diseases that are widespread in developing countries, risk the introduction of substandard and counterfeit medicines, and somehow fail to improve access to essential drug care. Incomes in developing countries, however, are too low to provide much of an incentive for research into drugs that meet their health needs. The higher cost of patented drugs as compared with generics reduces access to essential drug care rather than expanding it. Why then does the industry argue against parallel imports and compulsory licensing?

Four industry concerns are important here:

- 1) setting precedents that could spread to middle income or even high income countries (particularly for parallel imports);
- 2) generics that might reveal the actual cost of drug manufacture, which could create problems in their domestic markets;
- 3) a preference for international aid organisations to pay for more expensive proprietary drugs; and
- 4) lower market growth for proprietary drugs in developing countries with rapidly growing incomes.

The industry thus provides two other solutions to drug access that would maintain TRIPs without resorting to finding “loopholes”. The first consists of voluntary price reductions and, under some conditions, to offer drugs at not-for-profit prices. Since 15 April 2001 several pharmaceutical firms, including Pharmacia, Bristol Myers Squibb, Merck, Roche, Boehringer Ingelheim, and Abbot, have agreed to offer HIV/AIDS drugs to developing countries at prices far below the US \$10,000-\$15,000 per year charged in developed countries. GlaxoSmithKline (GSK) offers all its anti-retrovirals (ARVs) and anti-malarial drugs at not-for-profit prices to the least developed countries (LDCs) in Africa, such as Chad and Malawi, and at reduced prices for developing countries, including South Africa, Zimbabwe and Botswana. (GSK Annual Review. 2001) In April 2001, GSK charged US \$730 per year for HIV/AIDS combination therapy in South

Africa for public patients and double that for private patients. Parallel imports would make such special contractual arrangements unnecessary.

Second, the industry donates some drugs for free for HIV/AIDS and other tropical diseases. The IFPMA estimates that industry donations to developing countries run at roughly US\$ 500 million per year, which is equivalent to 0.14 per cent of global pharmaceutical sales.² Pfizer for example donates diflucan for opportunistic AIDS infections, Novartis donates multi-drug therapy for leprosy and GSK provides albendazole for lymphatic filariasis. Other large pharmaceutical firms have also "adopted" a tropical disease and have run programs to completely eliminate or control these diseases over a reasonable time frame. Aventis has a program to combat tuberculosis in South Africa, Pfizer runs a global drug donation program for Zithromax to treat trachoma, Merck donates Mectizan for river blindness, and Roche has a program to combat vitamin A deficiency.

These and other industry programs are welcomed by NGOs and the governments of developing countries. However, the industry offer of philanthropic donations and discriminatory pricing leaves discretionary control over supply and drug prices in their hands. The NGOs would prefer to have a competitive drug market to drive prices as low as possible. Both parallel imports and compulsory licensing have the potential to do this.

Generic firms offer ARV combination therapies at some of the lowest prices available. For example, Far-Manguinhos of Brazil offers a combination therapy of AZT, 3TC and Nivirapine at US\$ 1.55 per day (US\$ 565.75 per year). Cipla of India has offered to provide combination therapy for US\$ 350 per year, although there are doubts about its ability to supply drugs at this price. Both the NGOs and the industry would likely agree that even the lowest cost generic ARVs are still too expensive for the majority of HIV/AIDS patients in Africa.

In addition to price, two other problems face generic production of ARVs or other drugs. One concerns quality guarantees. The pharmaceutical industry argues that generics are of poorer quality and may lack bio-equivalence. The WHO has acted to solve this problem by testing the quality of generic drugs. On 21 March 2002, the WHO released the first list of manufacturers of safe generic AIDS drugs.

Another issue that has not been resolved concerns access to drugs by developing countries that lack the capability to make drugs. Under TRIPs, countries can only offer compulsory licenses to domestic firms. Several countries, including the US, blocked a solution to this problem at Doha that would have permitted countries with generic manufacturers to export generic drugs. In the absence of imported generics, developing countries are obliged to rely on price reductions offered by the main pharmaceutical firms. A decision on exports of generics is expected by the end of 2002 and is likely to be hotly contested. In the meantime, large pharmaceutical firms have already signed agreements with Senegal, Uganda, Rwanda, Ivory Coast and Cameroun to provide steeply discounted HIV/AIDS drugs.

■ Developing New Drugs

The second problem is a lack of drugs to treat many diseases that are widespread in developing countries but rare in the developed world. These are referred to as "neglected diseases". Between 13 and 16 new drugs have been developed for tropical diseases in the last 25 years, compared to 1,380 drugs for diseases that also occur in developed countries (Pécoul *et al.* 2001). A study of patents and citations for tropical diseases between the 1970s and the mid-1990s found that these never exceeded more than 0.5 per cent of all pharmaceutical patents. (Lanjouw and Cockburn 2001).

One of the promises of TRIPs is that it would provide a stronger incentive for pharmaceutical firms to invest in research on drugs to treat neglected diseases. The steadfast position of the industry is that any dilution of TRIPs will substantially reduce these incentives. This position has also been articulated forcefully by the US, Australia, Canada, Japan and Switzerland.

The NGOs are in partial agreement, noting that stronger patent protection in developing countries would have benefits if it spurred large pharmaceutical firms to develop drugs for neglected diseases at a reasonable cost, and if it provided incentives for indigenous generic pharmaceutical firms, such as Cipla in India, to develop innovative drugs for both the domestic market and for export.

Lanjouw (2001) has proposed a simple change to patent rules within the Organisation for Economic Co-operation and Development (OECD) that might

resolve some of the problems noted above. Firms would be able to choose to patent drugs in either developed or developing countries, but not in both. Drugs for diseases that are prevalent in the developed world, such as HIV/AIDS, cancer, and cardiovascular diseases, would rarely if ever be patented in developing countries, leaving them open to generics. Even if this solution were to win the support of developed countries, it does not provide new incentives to overcome the lack of attention by large pharmaceutical firms to doing research on neglected diseases in developing countries.

NGOs thus support some form of international funding for not-for-profit research into drugs for neglected diseases, plus programs to develop the research and development capability of developing countries. The likelihood of success in these initiatives would increase if major pharmaceutical firms had incentives to participate, bringing with them their expertise in drug screening, genomics and biotechnology. New initiatives, such as the Drugs for Neglected Disease Initiative – launched by the Paris-based NGO Médecins Sans Frontières with the backing of the Pasteur Institute of France, Brazil's Oswaldo Cruz Institute, the Indian Council of Medical Research, the Science University of Malaysia and the WHO with support from GSK – may provide a model of how this could be done.

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Endnotes

1 PhRMA. 14 November 2001. WTO Doha Declaration reaffirms value of intellectual property protection. <http://www.phrma.org/press/newsreleases/2001-11-14.310.phtml>.

2 PhRMA. 14 November 2001. *op cit*. It is not clear from the press release if the total includes funding by partnership agencies such as the UN and governments.

References

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IMPLICATIONS OF THE CBD FOR HEALTH AND BIOPHARMA

Building local capacity for research on drugs based on natural products¹ provides a complementary avenue to meet local health care needs. Medicines derived from natural products still make a significant contribution to the medicine cabinet. Annual global sales of pharmaceuticals derived from genetic resources lie between US \$75 and \$150 billion and of botanical medicines between US \$20 to \$40 billion. (ten Kate and Laird 1999) A recent, striking example of a naturally-derived blockbuster drug is *Taxus baccata*, from which the anti-cancer drug taxol is manufactured. Marketed by Bristol-Myers Squibb, under the brand name Paclitaxel, worldwide sales from 1998 to the third quarter of 2001 were US \$5.3 billion.²

A series of studies from the late 1990s confirm the continuing importance of biodiversity to health. Grifo *et al.* (1996) analysed the top 150 proprietary drugs from the US National Prescription Audit for the period January-September 1993. The audit is a compilation of virtually all prescriptions filled in the US during this time and the data are based on the number of times a prescription was filled. They found that 57 per cent of the prescriptions filled contained at least one major active compound "now or once derived or patterned after compounds from biological diversity". Cragg *et al.* (1997) analysed data on new drugs approved by either the US FDA or comparable entities in other countries between 1985-95, focusing on areas of cancer and infectious diseases. Of the 87 approved cancer drugs, 62 per cent are of natural origin or are modeled on natural product patents, and of the 299 anti-cancer drugs in pre-clinical or clinical development, the figure was 61 per cent. Newman and Laird (1999) demonstrated that the contribution of natural products to sales in the world's top pharmaceutical companies ranged from 10 to over 50 per cent.

Natural products may not maintain this market share in the future. During the 1990s, new technologies such as combinatorial chemistry, high-throughput screening and laboratories-on-a-chip provided unprecedented numbers of compounds to test and better ways to convert the resulting knowledge into synthetic molecules and those produced by biotechnology for testing. By comparison, natural products are often seen as too slow, costly