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Introduction

Essential medicines are those that satisfy the priority health care needs of the population. Between 1.3 and 2.1 billion people remain without access to them despite decades of effort (WHO 2004a). Improvement is slow: the proportion of the world's population with access to essential medicines, defined in Box B2.1, improved from an estimated 63% to only 70% between 1987 and 1999. Almost 80% of those without access live in low-income countries, and 20% in middle-income countries. Such figures conceal major differences within countries, and do not adequately convey a sense of which medicines are lacking. Annual expenditure on medicines in 2000 varied from US\$ 396 per head in high-income countries to only US\$ 4 in low-income countries. At the same time, medicines accounted for a higher percentage of total health expenditure in low-income (19%) and middle-income countries (25%) than high-income countries (14%).

Box B2.1 The concept of essential medicines

Essential medicines, according to WHO, are those that satisfy the priority health care needs of the population, with due regard to evidence on efficacy and safety, and comparative cost-effectiveness. They are intended to be available at all times in the context of functioning health systems, in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at an affordable price (WHO 2004b).

Countries and health care systems should apply these principles to select a list of essential medicines, linking it to evidence-based treatment guidelines, for use in professional training, supervision and audit.

The impact of an essential medicines list depends on how the health system is structured and governed. In most countries the ministry of health can use regulatory procedures to ensure that all public sector providers adhere to it and its accompanying rational treatment guidelines. However, this may be subverted in systems with a large and unregulated private sector. The lists can also be used by insurance agencies to set standards and guidelines for reimbursement or coverage of care.



Figure B2.1 The mismatch between expenditure on medicines and health need (*Source*: McCoy 2003)

The deeply unjust mismatch between expenditure on medicines and health need (Figure B2.1) mirrors global socio-economic disparities. 42% of global expenditure on medicines is spent on 5% of the world's population living in North America, while only 20% is spent on the majority of the world's population with the highest burdens of disease in Africa, Asia, the Middle East and Latin America.

Critics claim that the high prices of patented drugs are not a major barrier to access. Many essential medicines that are cheap and off-patent remain unavailable or inaccessible to millions of people, primarily a reflection of impoverished health care systems and communities. However, for millions of people, the lack of access to essential medicines is also a function of excessively high prices – as illustrated by the high prices of patented antiretroviral medicines.

Escalating levels of expenditure on medicines may reflect high volumes, high prices, inappropriate choices and irrational prescribing. For example, in Canada, the medicines share of total spending grew from a low of 8% in the late 1970s to 16% in 2002. A similar trend is evident in the health care system in the US, where medicine costs may soon exceed payments to doctors as the largest item on the health bill after hospital costs.

Finally, as new diseases and health threats emerge and pathogens develop resistance to medicines, and because many existing essential medicines are toxic or limited in their effectiveness, access to essential medicines is also determined by the success or otherwise of the research and development (R&D) of new medicines. The presence of so many prevalent and serious diseases without effective and affordable treatment (see Box B2.2) demonstrates a major failure of the pharmaceutical R&D system.

This chapter looks at three important issues related to the pharmaceutical sector. The first is the international intellectual property rights system and other trade-related impediments to access and rational medicine use. The sec-

Box B2.2 Drugs for neglected diseases

Despite advances in science, technology and medicine, the largely marketdriven system for allocating resources to pharmaceutical research and development ignores diseases that affect the poor, including several that constitute a significant portion of the global burden of disease. Instead, the system is more geared towards directing investment towards new and expensive 'lifestyle' medicines such as Viagra, which claim to address the needs of the affluent minority of the world's population. Global and national strategies to correct this market failure are therefore necessary.

The pipeline of drugs for neglected diseases has been virtually empty for decades. Only 16 of the 1393 new chemical entities (drugs or medicines) registered in the US and Europe in 1975–1999 were for 'tropical diseases' that afflict people in developing countries, and five of them emerged from veterinary research. The result is a critical shortage of effective drugs for many diseases that mainly affect the poor, such as leishmaniasis, Chagas disease, trypanosomiasis (sleeping sickness), malaria and TB.

Existing medicines may be excessively toxic, difficult to administer or too expensive. For example, leishmaniasis, which is endemic in 88 countries and affects an estimated 12 million people, with 1.5–2 million new cases annually, is mainly treated with pentavalent antimony. This drug, discovered a century ago, has serious side-effects, requires prolonged treatment and is losing its efficacy in some regions due to increasing parasite resistance.

Owing to individual or governmental lack of funding to purchase them, some medicines have been withdrawn from the market despite the need for treatment, e.g. effornithine for African sleeping sickness. Continued access to this was only facilitated when it emerged that it could also be used in an unrelated condition prevalent in developed countries, hence providing an economically viable market. (*Source* Trouiller et al. 2002)

Box B2.3 'Big Pharma' - profits and power

'Big Pharma' is a collective term used to describe the world's major pharmaceutical corporations, which are hugely influential in the control of the trade in medicines, and in shaping global trade rules and regulations. They include Pfizer, Bristol-Myers Squibb, Bayer, Merck, Pharmacia, Johnson & Johnson, Abbott Laboratories, Novartis, American Home Products, Eli Lilly, Schering-Plough, GlaxoSmithKline and Allergan.

The combined worth of the world's top five drug companies is twice the combined GNP of all Sub-Saharan Africa, and their influence on the rules of world trade is many times stronger because they bring their wealth to bear directly on the levers of western power. Their role in shaping international rules on patents by working hand in hand with the US government and European Commission has been extensively documented (Drahos and Braithwaite 2004).

Pharmaceutical profits, whether calculated as a percentage of assets or as a percentage of revenues, are among the highest of any commercial sector. The combined 2002 profits of the 10 biggest pharmaceutical companies, listed in *Fortune* magazine's annual review of the largest US businesses, were US\$ 35.9 billion – comprising more than half the US\$ 69.6 billion profits netted by the entire roster of Fortune 500 companies. These profits are reflected in the incredible earnings of top executives. For example, the former chairman and CEO of Bristol-Myers Squibb made US\$74,890,918 in 2001, not counting his US\$76,095,611 worth of unexercised stock options (Families USA 2001).

With such profits at stake, it is no surprise Big Pharma invests a huge amount of money in protecting them. Drug companies have the largest lobby in Washington, and contribute copiously to political campaigns. Well over \$100 million went to paying for issue ads, hiring academics, funding non-profits and other activities to promote the industry's agenda in Washington (Public Citizen 2003). In 2002, the drug industry hired 675 different lobbyists from 138 firms – nearly seven lobbyists for each US senator. Drug industry lobbyists include 26 former members of Congress and all told, 342 of them have 'revolving door' connections with the federal government.

ond is the corrupting influence of profit-driven pharmaceutical companies on health professionals, academics and regulatory bodies. The third is the need to reshape the way pharmaceutical R&D is funded and incentives offered. The chapter recognizes that the pharmaceutical sector has largely been shaped by a powerful and politically influential corporate sector intent on protecting its own interests (see Box B2.3). Civil society needs to mobilize when these interests conflict with the social aims of equity and health for all, and the chapter concludes with recommendations for action.

Intellectual property rights, monopolies and high prices

The price of new medicines is largely governed by an intellectual property rights (IPR) regime that grants patents to any company that registers a new medicine. Patents are granted by governments and give a company monopoly power to manufacture and sell a medicine free of competition from any other manufacturer in that particular country. This monopoly power allows the patent-holder to set a price many times greater than the cost of production. Patents are usually granted for a fixed period after which other companies are permitted to manufacture generic versions of the same medicine.

Big Pharma argues that patents are vital incentives to companies to invest in pharmaceutical research and development. It also says the revenue from profitable products can be used to support research into new treatments for diseases, 'including those which particularly affect the developing world' (IF-PMA 2005).

Initially, IPRs were governed internationally by the Paris Convention and administered by the World Intellectual Property Organization (WIPO). However, in 1986, the developed countries, led by the United States, brought IPR issues into the realm of trade policy and negotiations. Although certain developing countries argued that IPRs were not free trade issues, the developed countries, supported by Big Pharma, pushed through the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) in 1994 under the auspices of the World Trade Organization (Drahos and Braithwaite 2004). Developing countries gave up their resistance to the Agreement in the face of the overwhelming influence of the US, EU and Japan. The power imbalance of negotiations is reflected by the fact that only about ten developing countries actually sent intellectual property experts to the TRIPS negotiations (Matthews 2002).

TRIPS stipulates that by January 2005, all member states of the WTO must grant patents on all medicines for a period of 20 years. Whereas patents were previously granted by governments on a country-by-country basis, there is now a single and standard patent agreement that applies to all countries. A particular concern is the potential impacts on countries, such as India and China, that are important sources of generic medicines, including antiretrovirals. There is presently a campaign against the amendment to Indian patent



7 Selling medicines at the back of a bus.

law which will potentially destroy the generic drugs manufacturing capacity in India (Sen Gupta 2005).

A degree of flexibility has been built into TRIPS, following intensive lobbying by civil society and some developing country governments. This led to Medicines

the fourth WTO ministerial conference adopting the Doha declaration on the TRIPS Agreement and Public Health in 2001 (WTO 2001). This says that TRIPS should be implemented in a manner that supports the right of countries 'to protect public health and, in particular, to promote access to medicines for all'. Paragraph 5 provides a list of policy flexibilities that can be used to overcome intellectual property barriers to access to medicines. It asserts the freedom of each member state to determine the grounds on which compulsory licences can be granted without the consent of the patent-holder, and confirms that the agreement in no way limits countries' capacity to allow parallel trade in patented medicines. (A compulsory licence is granted to allow a third party to manufacture a patented product without the authorisation of the right holder; a parallel import is a good sold by the patent-holder and resold in another country without the patent-holder's permission.) Finally, the Doha declaration extended the deadline for TRIPS compliance for the 30 least developed countries until 2016.

The Doha declaration left one issue unresolved. A country without local manufacturing capacity would not be able to make use of a compulsory or government-use licence to improve access to medicines (Correa 2002). The WTO therefore decided in 2003 to allow for a temporary waiver of the requirement that medicines produced under a compulsory licence should be predominantly for the domestic market (Correa 2004). With this waiver, a compulsory licence could be granted to a company to manufacture generic versions of a medicine for export to another country. For this to happen, two compulsory licences may be required, one each in the importing and exporting countries.

In practice it is difficult for developing countries to make use of these flexibilities (Baker 2004a, DFID 2004). To start with, a variety of burdensome administrative tasks have been created to limit the potential for compulsory licensing (Baker 2003). According to 20 civil society groups, WTO took a 52– word mechanism endorsed by the EU in 2002 and created a 3200–word maze of red tape 'plainly designed to frustrate and undermine the objective of protecting public health and promoting access to medicines to all' (Joint NGO Statement 2003).

Developing countries are furthermore subjected to enormous economic and political pressures not to use the TRIPS flexibilities. These pressures include threats of litigation by companies and trade sanctions by governments. The US government, for example, has used bilateral trade agreements, the threat of sanctions, and associated diplomatic and political pressures to undermine countries that produce generic medicines and/or consider importing them (Oxfam 2002).

TRIPS-plus

The TRIPS agreement, despite the flexibilities permitted by the Doha declaration and the 2003 WTO decision, has harmed efforts to improve access to essential medicines. Even worse has been the development and implementation of a variety of 'TRIPS-plus' agreements and policies aimed at killing off the flexibilities and eroding further the capacity of governments to regulate the pharmaceutical sector and the price of medicines.

US bilateral policy on patents and medicines is hugely influenced by the giant pharmaceutical companies' quest to stave off generic competition for lucrative patented drugs (Oxfam 2002), and the US has pursued a TRIPS-plus

Box B2.4 The US-Australia free trade agreement

The free trade agreement between Australia and the US undermines Australian public health while protecting US pharmaceutical corporate interests. It prohibits compulsory licensing except in three circumstances, whereas TRIPS permits compulsory licensing in any circumstances if certain conditions are met (Drahos & Henry 2004). Another stipulation involves patent term extensions for pharmaceuticals beyond those required by TRIPS. The agreement also gives patent owners greater control over the importation or reimportation of their products to obstruct parallel importation, unlike TRIPS, which expressly steers away from setting a standard on parallel trade.

Australia's pharmaceutical benefits advisory committee recommends the listing of medicines that will be subsidized by a programme operated by the federal government. Pharmaco-economic analysis and reference pricing are used to determine the benefits of a new drug while monopsony power (where the product is bought or used by only one customer) is used to counter the price-setting monopoly power of pharmaceutical patentholders. As a consequence, medicine prices obtained by the Australian pharmaceutical benefits scheme are 3–4 times lower than those in the US (Lokuge et al. 2003). However, under pressure from US trade negotiators, the Australian government has agreed to the creation of an independent review body to examine medicines rejected by the committee. This follows a longer history of aggressive action by US pharmaceutical companies, including legal challenges to the committee's decisions and politicallobbying for removal of committee members (Henry & Birkett 2001). agenda through a series of bilateral and regional trade agreements (MSF 2004). These include free trade agreements (FTA) with the Americas, Central America, Jordan, Singapore, Chile, Australia and Morocco. The US is now negotiating an agreement with Thailand, opposed by Thai civil society, whose TRIPS-plus provisions will obstruct affordable antiretroviral treatment for nearly 10,000 people with AIDS. An agreement is also under negotiation with the Southern African Customs Union.

TRIPS-plus agreements and policies include limiting the potential for governments to award compulsory licences and embark on parallel importing. Another stipulation involves patent term extensions beyond those required by TRIPS. They are also being used to slow down access to generic medicines by conferring exclusive rights to pharmaceutical companies for the patient data used to secure regulatory approval. Although the TRIPS agreement is not overly prescriptive on protection of undisclosed data submitted to regulatory authorities by manufacturers, US bilateral trade agreements include granting exclusive rights on these data for at least five years. Since generic manufacturers rely on pharmaceutical test data to demonstrate that their products are safe and effective, data exclusivity means that they will have to repeat many costly clinical trials when they want to register a new generic medicine. This will significantly delay the introduction of generics even when there are no patents in effect.

Finally, bilateral trade agreements are being used to erode the power and role of national authorities for the regulation of medicines and the structures responsible for medicines selection. Regulation of medicines is one of the most important health stewardship functions of government. An effective framework should include a competent process for ensuring that medicines that are produced, sold and dispensed are safe and effective; that monitoring and surveillance systems exist to identify problems with safety; and that clinical trials conducted by the pharmaceutical sector are ethical, transparent, methodologically sound and free of bias. As outlined before, a complementary process involves those structures that ensure that the clinical use of medicines is informed by the periodic development and updating of treatment guidelines and essential medicines lists.

Such a framework should apply to both brand and generic medicines, and needs to be efficiently managed and robust enough to withstand pressure from pharmaceutical manufacturers, insurance companies and treatment activist groups alike. The challenges facing developing country regulators are particularly acute given neoliberal reforms and the lack of public sector capacity (Hill and Johnson 2004). The use of trade agreements to undermine public health and governments' regulatory capacity is particularly worrying given growing evidence that Big Pharma routinely places profit margins above the imperative to protect patient safety, and has become a corrupting influence on public health, academic and clinical practice. These issues are discussed later.

Dispelling the myth that patents promote efficient and innovative pharmaceutical R&D

Pharmaceutical companies repeatedly claim that patent protection is 'the goose that lays the golden egg' – that the companies' monopoly power is a price worth paying because it leads to new medicines. However, this argument is built on a number of myths that, when exposed, point to a moral and logical need for fundamental reform of how pharmaceutical research is financed and rewarded.

Firstly, Big Pharma portrays its industry as a highly risky one in a competitive market, just able to cover its enormous R&D costs but managing

How much does it really cost to manufacture a drug? In November 2001, the Tufts Centre for the Study of Drug Development, which is 65% funded by the industry, came out with a figure of \$802m. Public Citizen, a consumer organisation, did a detailed analysis of the figure and concluded that it was inflated by about 75%. In addition, none of the 68 drugs Tufts considered had been developed with

the help of government money, unlike the case with many other medicines.



Figure B2.2 How much does it cost to develop a new medicine? (Source: Guardian 2003)

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nonetheless to deliver a stream of innovative medicines in the public interest. However, as mentioned earlier, their profits are substantial. Pharmaceutical companies have also been guilty of exaggerating the cost of developing a new medicine (see Figure B2.2).

Furthermore, much of the truly innovative research that feeds into the manufacture of medicines is not undertaken by the corporate sector but by publicly funded research institutions and universities. Nearly half of the biomedical research spending in the United States is supported by either the government or non-profit sector, the outputs of which enter the public domain to the benefit of the commercial sector. Others were first developed by smaller biotech companies and then licensed to the large companies.

In contrast, a system which relies only on patent protection to fuel innovation can easily become distorted and inefficient (Baker and Chatani 2002). First, patent protection encourages an overemphasis on the production of copycat drugs that add little value to health outcomes. The US Food and Drug Administration said 76% of the drugs it approved in the 1990s were duplicative rather than breakthrough drugs (US Food and Drug Administration 2001). Second, patent protection gives manufacturers a big incentive to persuade doctors and patients to use their medicines rather than others – resulting in high spending on marketing and over-prescribing. Third, the legal and lobbying costs associated with securing and enforcing patents, which can include side

PhRMA Initiatives	Budget (US\$m)
Pharmaceutical lobbying at the US federal and state level	121.4
Fighting price controls and protecting patent rights in foreign countries and in trade negotiations	17.5
Fighting a union-driven initiative in Ohio to lower drug prices for people with inadequate insurance cover	15.8
Lobbying the US Food and Drug Administration	4.9
Payments to research and policy organizations sympathetic to the industry	e 2.0
Funding a standing network of economists to speak against US d price controls	rug 1.0
Changing the Canadian health care system	1.0
TOTAL	163.6

 TABLE B2.1 Spending money to change policy: Pharmaceutical Research and

 Manufacturers of America budget initiatives

Source: Pear 2003

payments to generic producers to keep competition out of the market, have become enormous (Box B2.3). The US industry recently spent US\$ 163 million in a year on trying to change patent laws across the globe (Table B2.1). Fourth, restricting the dissemination of research findings is another cause of inefficiency – scientific progress is impeded by the financial incentives to prevent the disclosure of research findings until patents are filed. Lastly, the existence of large mark-ups provides a strong incentive for the production of unauthorized medicines. When medicines can be manufactured at prices between a tenth and a hundredth of the patent-protected price, there are enormous incentives to make black-market versions or counterfeits.

In contrast, alternative incentive systems for research continue to be effective and efficient. Innovative, high quality scientific developments can flourish for the benefit of all with good management and leadership (Baker 2004). The Human Genome Project shows that with good management and leadership; clear plans and goals; regular inter-action between funders, managers and technical experts; and a competitive atmosphere with peer review, open data and information exchange, researchers on academic salaries in the public domain can produce innovative and high quality scientific developments for the benefit of all (also discussed in part B, chapter 5).

The corruption of ethics and trust

There is growing concern about Big Pharma's unethical behaviour and lack of transparency. It is increasingly entering into financial arrangements with academic and research institutions that threaten the objectivity and credibility of clinical research (Medawar and Hardon 2004). In contracts with academic researchers, the companies may insist on controlling how the research is done and reported, and whether the results will be published. Furthermore, a growing number of clinical trials are being managed by investor-owned businesses that are even more beholden to the drug companies because the companies are their only clients.

The contact between pharmaceutical companies and researchers has become pervasive, as shown by the decision by the highly respected *New England Journal of Medicine* to drop its requirement that authors of review articles of medical studies must not have financial ties to the companies whose medicines were being analysed (Drazen and Curfman 2002). The journal could no longer find enough independent experts. The new standard is that reviewers can have received no more than US\$10,000 from companies whose work they judge. Many see this as an unacceptable compromise, evidence of a scientific establishment corrupted by bias and conflicts of interest. In addition, this Health care systems | B2

decision only applies to review articles. The authors of scientific studies are often funded by private drug companies with a stake in the results.

In other cases, papers are ghost-written by pharmaceutical company staff or contractors. Scientists at universities are often allowed to have stock options in companies benefiting from the research they are conducting. Researchers on industry payrolls may be persuaded to suppress unwanted results, and those who defy their corporate sponsors may lose their funding. Lastly, where university research was once oriented to producing independent and public knowledge, it is now increasingly locked up in patents.

This type of corruption and bias also extends to prescribing doctors and medicine regulatory authorities (Angell 2004, Avorn 2004, Kassirer 2005). Big Pharma spends lavishly to influence doctors who write the prescriptions. It funds and thereby influences much of the continuing medical education doctors need to renew their licences, and subsidizes scientific meetings of medical societies where it hawks its wares and often sponsors its own programmes.

Pharmaceutical companies have also been able to purchase influence in regulatory bodies: half the US Food and Drug Administration's budget for evaluation of new drugs comes from pharmaceutical company user fees, making it dependent on the industry it regulates – an obvious conflict of interest. A significant number of staff in regulatory authorities also have long and close connections with the pharmaceutical companies. The executive head of the regulatory authority in the UK, for example, was an employee of SmithKlineBeecham for over 20 years.

Even more alarming is the absence of effective laws and regulations to force drug companies to reveal all their clinical trial data. The FDA and its European counterparts have no right to demand to see any data that drug companies do not wish to reveal. This selective and biased release of scientific data, which should be made illegal, is potentially harmful to patients and also has a corrosive effect on the ethics and values of scientific inquiry. Regulatory bodies are also under political pressure to speed up the licensing of new medicines in order to minimize the loss of potential profits due to delays in marketing a new drug.

Proposals for a new agenda

TRIPS and international trade agreements Intellectual property rights related to essential medicines and other essential health technologies should not be governed by the WTO and trade agreements, but by public health considerations and public health institutions – elevating human rights and social considerations above the narrower considerations of commercial trade. In



8 Informal supply: lack of regulation of pharmaceutical markets is a key problem for many poor countries.

the long term, civil society should work towards the annulment of the TRIPS agreement related to medicines and the creation of a more just framework. Similarly, civil society and health professional associations should campaign

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for the annulment of all TRIPS-plus agreements and policies related to medicines in bilateral and regional trade agreements.

In the interim, NGOs and health agencies must work with governments to make maximum use of the existing TRIPS flexibilities. Countries exempt from being TRIPS-compliant until 2016 must not be pressurized into introducing new patent laws before then, or enacting new laws that undermine their capacity to make use of the flexibilities, as some are doing. Governments have a better chance of withstanding pressure from Big Pharma and the political establishments of the US and EU with public support and civil society involvement. Efforts are also required to develop governments' technical and legislative capacity.

Keeping the generic supply pipeline open The generic medicine manufacturing capacity in countries such as India, China, Brazil and Thailand must be maintained. The application of the TRIPS flexibilities is one important mechanism. Continued support must be given to WHO's efforts in pre-qualifying quality products and producers so as to speed up the process by which generic medicines can be registered for use in countries. So far, the WHO system has proved effective and efficient.

The administrative and paperwork requirements for the TRIPS compulsory licensing flexibilities should also be streamlined, particularly in cases where the response to public health emergencies can be strengthened by rapidly increasing access to generic medicines. WHO could be funded to provide advice and assistance to countries needing to use the flexibilities.

A new paradigm for funding and stimulating pharmaceutical R&D New ways to fund and stimulate pharmaceutical R&D are needed to achieve the goal of universal access to essential medicines and avoid the huge inefficiencies and corruption of the current system. Four innovative proposals could stimulate R&D while reducing the difference between the sales price and actual cost of production (Baker 2004b). These are:

- a mandatory employer-based research fee to be distributed through intermediaries to researchers;
- zero-cost compulsory licensing patents, in which the patent-holder is compensated based on the rated quality of life improvement generated by the drug, and the extent of its use;
- an auction system in which the government purchases most drug patents and places them in the public domain; and

• financing pharmaceutical research through a set of competing, publicly supported research centres.

These proposals could remove the need for excessive spending on marketing, provide adequate financing for expensive biomedical research, reduce incentives for wasteful copycat research and for data protection and scientific secrecy, minimize the risk of political interference in setting research priorities, and be administratively feasible at the international level.

A proposed Medical Research and Development Treaty, which proposes a new paradigm that includes minimum national obligations for supporting medical R&D, with flexibility regarding the business models and intellectual property rules, should be supported (http://www.cptech.org/workingdrafts/ rndtreaty.html, accessed 8 March 2005).

More directly, the Drugs for Neglected Diseases Initiative (http://www.dndi. org, accessed 8 March 2005) aims to raise financing directly to build a balanced research portfolio of long, medium and short-term projects to fill identifiable gaps in the drug development pipeline for key neglected diseases.

Strengthen the transparent and ethical regulation of pharmaceutical companies Profit-motivated pharmaceutical companies, whether Big Pharma or generic manufacturers, cannot be left to operate without a strong regulatory framework to promote rational medicine use and patient safety. The erosion of independent national and international regulatory structures and powers must be reversed. Civil society must play a further watchdog role that holds pharmaceutical companies and government regulators accountable to high standards of ethical practice. WHO, working in collaboration with NGOs such as Health Action International and Public Citizen, should produce a periodic scorecard of the competence and probity of national medicine regulatory bodies as a mechanism for monitoring progress.

Laws, policies and agreements should be established to make the full disclosure of all clinical trials data an obligation. Failing this, any breaches of patient safety arising from the deliberate disclosure of clinical trials data should be treated as criminal acts and be prosecuted.

Legitimize price control options Domestic regulations to control drug prices are an important mechanism to promote access. In countries where public expenditure on health care is relatively high, government- or public-funded health insurance can keep medicine costs low by negotiating cheaper prices with pharmaceutical manufacturers. In countries where public health

expenditure is low, retail sales constitute the majority of pharmaceutical sales and direct price control mechanisms are necessary to place a ceiling on profitability, unit prices or distribution chain costs. However, such interventions are under attack as part of the neoliberal drive to deregulate the sector and weaken the monopsony power of governments (the power of a large buyer to negotiate lower prices). In India, a country with low public expenditure on health care, the number of medicines under price control declined from 342 in 1979 to 73 in 1995, and there is a proposal to reduce it further to 25. Such trends need to be reversed and governments need to be proactive to stabilize medicine prices.

End the corruption of academic research institutions As public institutions of learning and inquiry, universities and research centres must be protected from the corrosive effect of commercial influences. As a first step in this direction, the US National Institutes of Health and the Canadian Institutes for Health Research have recently commissioned studies to assess the integrity of clinical research in their countries and make policy suggestions for its preservation and enhancement. Similar initiatives should be widely supported, and their recommendations given serious consideration.

Revitalize Essential Drug Programmes The term 'essential drug programme' (EDP) was common in the international health literature 20 years ago, when countries were encouraged to set up national committees to define costeffective treatment guidelines as a means of promoting rational prescribing. Today health sector reform, neoliberal deregulation and the commercialization of health care systems have resulted in a more market-driven pattern of medicine prescribing. As a consequence there is over-prescribing (with growing costs, a growing incidence of negative side-effects and the development of antimicrobial resistance) and inefficient prescribing (using more expensive medicines when cheaper versions would do). It is time for WHO to revitalize the essential medicines concept and find ways of integrating it in increasingly fragmented and commercialized health systems. Consumer and health professional organizations should insist on independent and periodic surveys of prescribing practices in public and private health care sectors.

References

Angell M (2004). *The truth about the drug companies: how they deceive us and what to do about it*. New York, Random House.

Avorn J (2004). *Powerful medicines: the benefits, risks, and costs of prescription drugs*. New York, Random House.

- Baker B (2003). *Vows of poverty, shrunken markets, burdensome manufacturing and other nonsense at the WTO* (http://www.healthgap.org/press_releases/03/092703_ HGAP_BP_WTO_Cancun.html, accessed 6 March 2005).
- Baker B (2004a). *Processes and issues for improving access to medicines: willingness and ability to utilise TRIPS flexibilities in non-producing countries*. London, DFID Health Systems Resources Centre.
- Baker D (2004b). *Financing drug research: what are the issues?* Washington DC, Center For Economic and Policy Research.
- Baker D, Chatani N (2002). *Promoting good ideas on drugs: are patents the best way?* Briefing paper. Washington DC, Center for Economic and Policy Research.
- Correa C (2002). *Implications of the Doha declaration on the TRIPS agreement and public health*. WHO/EDM/PAR/2002.3. Geneva, WHO.
- Correa C (2004). Implementation of the WTO general council decision on paragraph 6 of the Doha declaration on the TRIPS agreement and public health. WHO/EDM/ PAR/2004.4. Geneva, WHO.
- DFID (2004). Access to medicines in under-served markets. What are the implications of changes in intellectual property rights, trade and drug registration policy? DFID/ HSRC overview paper. London, DFID Health Systems Resources Centre.
- Drahos P, Braithwaite J (2004). Who owns the knowledge economy: political organizing behinds TRIPS. Corner House briefing 32 (http://www.thecornerhouse.org. uk/item.shtml?x=85821, accessed 6 March 2005).
- Drahos P, Henry D (2004). The free trade agreement between Australia and the United States. *British Medical Journal*, 328:1271–2.
- Drazen J, Curfman G (2002). Financial associations of authors. *New England Journal of Medicine*, 346:1901–2.
- Families USA (2001). *Off the Charts: Pay, Profits and Spending in Drug Companies* (http://www.familiesusa.org/site/PageServer?pagename=media_press_2001_ drugceos, accessed 6 March 2005).
- *Guardian* [anonymous] (2003). How much does it really cost to manufacture a drug? *Guardian* Special report: AIDS. London, *Guardian*, February 18 (http://www. guardian.co.uk/aids/graphic/0,7367,898105,00.html, accessed 14 March 2005).
- Henry D, Birkett D (2001). Changes to the pharmaceutical benefits scheme. *Medical Journal of Australia*, 74:209–210.
- Hill S, Johnson K (2004). *Emerging challenges and opportunities in drug registration and regulation in developing countries*. London, DFID Health Systems Resources Centre.
- IFPMA (2005). *Intellectual Property and Patents*. International Federation of Pharmaceutical Manufacturers and Associations, Geneva (http://www.ifpma.org/Issues/ issues_intell.aspx, accessed 6 March 2005).
- Joint NGO Statement on TRIPS and public health. WTO deal on medicines: a 'gift bound in red tape' (2003) (http://www.cptech.org/ip/wto/p6/ngos09102003.html, accessed 6 March 2005).
- Kassirer J (2005). On the take: how medicine's complicity with big business can endanger your health. Oxford, Oxford University Press.
- Lokuge B, Faunce T, Denniss R (2003). *A back door to higher medicine prices? Intellectual property and the Australia-US Free Trade Agreement*. Canberra, The Australia Institute.
- Matthews D (2002). *Globalising Intellectual Property Rights: The TRIPS Agreement*. London, Routledge.

Medawar C and Hardon A (2004). Medicines out of control? Netherlands, Aksant.

- MSF (Médecins sans Frontières) (2004). *Access to medicines at risk across the globe: what to watch out for in free trade agreements with the United States*. Briefing note (http://www.accessmed-msf.org/documents/ftabriefingenglish.pdf, accessed 6 March 2005).
- McCoy D (2003). *Health sector responses to HIV/AIDS and treatment access in southern Africa: addressing equity.* Discussion Paper 10. EQUINET (http://www.equinet africa.org, accessed 14 February 2005).
- Oxfam (2002). *US bullying on drug patents: one year after Doha*. Briefing paper 33. Oxford, Oxfam.
- Pear R (2003). Drug companies increase spending on efforts to lobby Congress and governments. *New York Times*, June 1 (http://www.nytimes.com/2003/06/01/ national/01LOBB.html?tntemail1, accessed 8 March 2005).
- Public Citizen (2003). *The Other Drug War 2003: Drug Companies Deploy an Army of* 675 Lobbyists to Protect Profits (http://www.citizen.org/documents/Other_Drug_War2003.pdf, accessed 6 March 2005).
- Sen Gupta (2005). *Indian Patent Act Jeopardising the Lives of Millions*. Bangalore (http://www.phmovement.org/india/articles/indianpatentact.html, accessed 6 March 2005).
- Trouiller P et al. (2002). Drug development for neglected diseases: a deficient market and a public-health policy failure. *Lancet*, 359:2188–2194.
- US Food and Drug Administration (2001). *NDAs approved in calendar years 1990–2001 by therapeutic potentials and chemical types* (http://www.fda.gov/cder/rdmt/pstable. htm, accessed 6 March 2005).
- WHO (2004a). The world medicine situation. WHO/EDM/PAR/2004.5. Geneva, WHO.
- WHO (2004b). *What are essential medicines?* (http://www.who.int/medicines/rationale. shtml, accessed 14 February 2005).
- WTO (2001). *Declaration on the TRIPS agreement and public health*. Fourth WTO ministerial conference, Doha, Qatar (http://www.wto.org/english/thewto_e/minist_e/ mino1_e/mindecl_trips_e.htm, accessed 6 March 2005).