

D4 | THE PHARMACEUTICAL INDUSTRY AND PHARMACEUTICAL ENDEAVOUR

The relationship between medicinal drugs and human health cannot be explained simply in terms of the policies and actions of ‘the pharmaceutical industry’, partly because the industry includes many different players, and partly because none of them operates in isolation. In one way or another, companies operate within a complex framework defined by their legal remit and market conditions, government and regulatory activity, professional standards and norms, and consumer expectation and demand. The relationship between medicinal drugs and human health is, therefore, best understood in terms of pharmaceutical endeavour.

The pharmaceutical industry comprises smaller and larger players, ranging from local to multinational enterprises. They may be centrally or peripherally involved in all or some of many overlapping activities, including research, development, testing, approval, distribution, and marketing of either branded or generic medications, and sometimes both.

In the context of world health, leadership of the industry rests mainly with the Big Pharmas, the top 20 or so multinational corporations with annual revenues measured in tens of billions of dollars. In 2007, some 61 companies had annual sales of over \$1 billion each (PRLog press release 2008). Between them, they control well over half of all world pharmaceutical trade and collectively have a dominant and growing influence over drug utilisation and regulation.

The nature of pharmaceutical endeavour and its impact on human health have changed dramatically over the past 100, 50, even 20 years, and, arguably, the rate of change is still increasing. Over the years, the industry, mainly the forerunners of the Big Pharmas of today, has provided many, sometimes remarkable, health solutions. More recently, however, there is increasing concern about diminishing health returns, even a reference to Pharmageddon, ‘the prospect of a world in which medicines and medicine produce more ill-health than health, and when medical progress does more harm than good’.¹

Health climate change

The tide turned probably around 1980, by which time it was clear that we had the technical capacity to check ill-health and relieve hunger on a global scale. The main missing ingredient was political will, but there was also much optimism that it might be found. With its campaign cry, ‘Health for all by the year 2000’, the World Health Organisation (WHO) set the tone.



40 Generic medicines shop in Chittorgarh, India: outcome of an innovative programme by the administration to promote generic medicines (Narendra Gupta)

In 1977, the WHO launched its policy on essential drugs, emphasising the possibility of transforming world health through the effective use of relatively few essential drugs. The medicines identified were overwhelmingly unbranded ('off-patent' and available in generic form) and represented only a small fraction of the many thousands of preparations that the pharmaceutical industry wanted to sell. Importantly, the concept of essential drugs made universal therapeutic sense, even if the need was greatest in developing countries.

The opposition of the pharmaceutical industry was inevitable, all the more so because of the growing realisation of what later became known as 'the crisis of productivity in drug innovation'. The first decade or two following the Second World War had proved to be a golden age of innovation, but thereafter came decline. The cost of innovation has since increased dramatically and the number of really indispensable new drugs has fallen (Medawar and Hardon 2004).

In response, the industry reacted, first by embarking on wave after wave of 'consolidation', growing through mergers and acquisitions into the Big Pharmas of today. Moreover, since around 1980 – thanks to the liberalisation of trade policies under the influence of Reagan, Thatcher, and others – the process of globalisation gathered momentum. That process may not be complete, but might still be described as mature.

The Big Pharmas otherwise responded to the crisis in innovation by greatly reducing investment in basic research and less profitable drug development.

At the same time, they hugely increased investment in drug marketing and in the intensive promotion of inessential (lifestyle) drugs in mass markets. That trend became especially obvious in the USA following the 1997 legalisation of direct-to-consumer advertising of prescription drugs.

National health and drug expenditure in the USA is now substantially higher than in any other country (e.g. twice that in the UK), but with no obvious effect on the classic health indicator, life expectancy. For all the benefits of the existing US health care system, most Americans are either obese or overweight, and only about 3 per cent of the US population is estimated to maintain a normal weight, eat a nutritious diet, take adequate exercise, and not smoke (Centers for Disease Control and Prevention 2001). At the same time, at least 15 per cent of the US population is completely uninsured, and just over one-third of the population is 'under-insured', unable to cover the costs of their medical needs.²

In contrast, WHO estimates that more than one-third of the world's population lacks regular access to the medicines it needs. In low-income countries, 10.3 million children under five years of age died last year; 8.6 million of these deaths could have been prevented if those at risk had had access to essential medicines (Medical Education Cooperation with Cuba 2010). Today, in 32 countries more than half the population lacks regular access to basic essential medicines. At the same time, over one billion people, one-sixth of the world's population, suffer from one or more neglected tropical diseases (WHO 2010). 'Neglected diseases' are those that disproportionately affect the populations of developing countries and which do not represent a commercially viable market for pharmaceutical companies, because those suffering generally cannot afford the drugs produced by these companies.

In short, and for all the progress made, under-medication remains an appalling problem in many parts of the world, while over-medication threatens others. Are these two world health crises related? In symbolic terms – like the contrast between obesity and emaciation from starvation – they clearly are. Beyond this, one may well conclude that excessive demand for medicines in richer countries perpetuates the growth of a global medicinal drug production system that by its nature neglects medical need where people cannot pay.

Over-medication is a world health problem too

To this extent, under-medication and over-medication seem to be two sides of the same coin. Therefore, one should ask whether, and to what extent, the problem of drug deprivation in developing countries might be addressed by curbing the extent of over-medication elsewhere.

There are three main reasons for focusing on the problem of over-medication. The first is simply to encourage a radical reappraisal of the impact of pharmaceutical endeavour on human health. The fact that life expectancy is unrelated to spending on health care underlines the need for this. Moreover,

abundant evidence from richer countries shows that the main determinants of health and mortality have far less to do with absolute levels of wealth and far more to do with equality of income distribution (Wilkinson and Pickett 2010).

Another reason would be to try to contain excessive and inappropriate industry influence. The point is further discussed below. Suffice it here to say that the dominant influence of the Big Pharmas has affected not only doctors' prescribing habits and patterns of consumption, but also the policies of national governments and health organisations, standards of drug approval,³ regulation and enforcement, and the thrust of international legislation on patent law and access to drugs.

The third main reason for focusing on over-medication as a world health problem is to gain a clearer understanding of the relationship between drug benefits and harms. The urgency of this task is underlined by the gross imbalance that exists worldwide between the resources made available for the investigation and reporting of the health benefits and harms that result from drug use. To date, we have yet to develop even a taxonomy, let alone appropriate procedures, to establish the true contribution of medicinal drugs to *ill-health*.

We have still barely advanced from the 1970s, when Illich and Thomas, among others, warned of the dangers that confront us now. The present lamentable state of public health in the USA suggests not only the need to beware of that country's model of health care as a template for other nations, but also the great importance of heeding Illich's warning to guard against the social and cultural iatrogenesis that would result in 'the paralysis of healthy responses to suffering, impairment and death' and lead to a disabling dependence on 'health care' (Illich 1976).

Thomas presciently anticipated the problem beyond that: whatever the gains, the combination of market forces and medical endeavour tends to destroy public health provision. The rising tide of over-medication is clearly linked to unsustainable demand. As Thomas warned 30 years ago:

The trouble is, we are being taken in by the propaganda, and it is bad not only for the spirit of society; it will make any health-care system, no matter how large and efficient, unworkable. (Thomas 1980)

In short, pharmaceutical endeavour has already reached the point at which the relevance of Pharmageddon might be real.

Values of the international pharmaceutical industry

The international industry, under the leadership of the Big Pharmas, walks tall, carries great weight, insists that it behaves responsibly, and is a driver of good health. On this basis, it enjoys a range of rights, privileges, and protections – and increasingly partnerships – granted not only by host governments, but also by health practitioners and professional associations.

Meanwhile, ill-health remains endemic and enduring in developing countries, and the mood of optimism that characterised the 1960s and 1970s has long since disappeared. Certainly, probably every major pharmaceutical company can point to philanthropic programmes and to worthwhile health initiatives in many different low-income countries. Still, the evidence overwhelmingly suggests both that not much is changing and that there is little reason to suppose it will. Existing systems of pharmaceutical endeavour do not and cannot prioritise the development of world health.

Pharmaceutical endeavour is naturally mainly geared to performance in major markets. Thus, while 10 key countries account for over 80 per cent of the global market, developing countries account for about 8 per cent (Holland and Bátiz-Lazo 2004). IMS Health estimated the value of the global pharmaceutical market in 2010 at over \$824 billion, with growth predicted at a 4–7 per cent compound annual rate through 2013 (Roner 2009). The style and policies of the Big Pharmas are framed accordingly.

In this context, it makes sense to look mainly to the USA to get some sense of the values that drive global pharmaceutical endeavour. Twelve of the 20 largest pharmaceutical and biotech companies (ranked by health care revenue) are US-owned and the USA on its own accounts for almost half of the global pharmaceutical market. Moreover, the annual Fortune 500 survey shows that the pharmaceutical industry is, and long has been established as, the most profitable of all businesses in the USA, routinely reporting double-digit returns on sales revenue.⁴

With earnings on this scale, the industry is well placed to invest massively in third parties, to spread influence, and to get its own way. Thus, the Center for Public Integrity records that the US pharmaceutical industry spent \$855 million, more than any other industry, on lobbying activities from 1998 to 2006 (*ibid.*). Payments to doctors – for research services and for drug promotion – are not generally disclosed, although some details are now emerging, both as a condition of legal settlements and by way of anticipating a requirement in the US Health Reform Act (2010), which will require companies, from 2013, to disclose and explain payments above \$10 made to doctors. Meanwhile, the US public interest group Pro-Publica (Journalism in the Public Interest) published in 2010 details of payments totalling \$258 million by seven companies, including the names of recipients (Nguyen et al. 2010).

The wealth of the Big Pharmas, not to mention their compliance record, is further underlined by the scale of the fines paid for illegal activities, especially in relation to drug marketing. The US Project on Government Oversight (2010) reported that since 2004 pharmaceutical companies had paid over \$7 billion in fines and penalties. The largest was the \$2.3 billion paid by Pfizer in September 2009 (*ibid.*) for illegally marketing the pain reliever Bextra (Valdecoxib) until 2005, when it was removed from the market owing to concerns about the risk of heart attack and stroke (Hepp 2010).

Such huge fines are neither exceptional nor as crippling as they might seem. The Alliance for Human Research Protection (2010) reports that every major company (Bristol-Myers Squibb, Eli Lilly, Pfizer, AstraZeneca, and Johnson & Johnson) selling ‘new generation’ anti-psychotic drugs has either settled a recent US government case for hundreds of millions of dollars, or is currently under investigation for possible health care fraud. Eli Lilly, for instance, paid a \$1.4 billion fine in 2009 for illegally marketing Zyprexa (olanzepine), but sales of Zyprexa just in 2008 were \$2.2 billion in the USA alone, and \$4.7 billion worldwide.

Big Pharmas operating in the USA also face substantial costs in settling civil actions in drug injury cases, not to mention the legal fees involved in trying to defuse them. Occasionally, details of a settlement may leak out, although binding secrecy is the general rule. Given the estimated scale of drug injury in the USA,⁵ clearly many more billions of dollars would be involved. Bloomberg reported that GlaxoSmithKline paid out \$1 billion in 2010 to settle about 800 claims relating to just one adverse effect (birth defects) of one of its drug products, Paxil (paroxetine).⁶ (See Box D4.)

The relevance of all this outside of the USA, and especially in developing countries, is not only that all such costs will be reflected in the price of medicinal products. The wider problem relates to the appropriateness and effectiveness of the predominantly US model of drug approval, use, and control, especially in countries with very limited resources and huge health needs. Would one expect Big Pharmas to behave any better in countries beyond their main markets, in the absence of a strong professional infrastructure, and when regulatory and enforcement capacity and provision for redress were conspicuously lacking? The notion that developing countries may benefit from the ‘higher’ standards required in high-income countries seems dubious when most countries have little or no effective regulatory capacity at all (WHO 2004).

For lack of drug regulation

The relevance of all this for developing countries is further underlined by a wealth of evidence that suggests that even in the highest-income countries, the regulators struggle to perform effectively and often fail. An important UK parliamentary inquiry in 2005 ‘revealed major failings in the regulatory system’, detailing concerns about the licensing process, including questions of access to generic drugs, the conduct of clinical trials, control of marketing, post-marketing drug safety evaluations, and product withdrawals. This inquiry reported not only ‘serious weaknesses’ in the regulatory system, but also that ‘the Agency seemed oblivious to the critical views of outsiders and unable to accept that it had any obvious shortcomings’ and that it failed to provide ‘the discipline and leadership that this powerful industry needs’ (Alliance for Human Research Protection 2010). Comparable weakness – ‘This agency can

be dangerous' – has been identified with regard to the US Food and Drug Administration (Angell 2010).

So it is that even in the most regulated environments, pharmaceutical companies routinely resort to a wide range of unsavoury and plainly unscientific practices whose effect is to move goalposts and tilt the pitch, and therefore to greatly distort understanding of drug benefit and risk.

Always with an eye to return on investment (ROI), companies generously fund university departments and chairs, sponsor professional and patient organisations, and support extensive CME (continuing medical education) programmes. In all of these ventures, industry self-interest and promotional messages are never far away.

Companies purchase not only political support and favours, but also the services of 'key opinion leaders', supposedly independent academics, clinicians, and others who are paid handsomely to give product presentations, to troubleshoot, and otherwise to make representations on behalf of the companies (Center for Public Integrity 2008). Conflicts of interest, let alone the details of the payments made, are often not disclosed.

For lack of effective regulation and various other reasons, the quality of *most* clinical trials (and therefore the reliability of their results) are never even adequate. Former editors of the *British Medical Journal* and the *New England Journal of Medicine* agree on this.

We reject over 90% of the papers submitted to us, primarily because the research is of poor quality. The design or methodology of the study may be inadequate to address the hypothesis, the analysis of the data may be inappropriate, the conclusions may not be supported by the data or the data may support alternative conclusions, and so forth. The possible flaws, many of them fatal, are virtually endless. (Angell and Blume 2000; Gore et al. 1992)

The editor of *The Lancet* told a UK parliamentary committee in 2005 that this kind of research would typically end up in the hands of medical publications that are, in fact, 'information laundering operations', in which compliant publishers gain from potentially huge kickback payments, or end up being threatened with terminal loss of business if they refuse to comply.

Beyond this, pharmaceutical companies routinely orchestrate the 'ghost-writing' of the results of clinical trials, employing professional writers to put a gloss on the results, then paying 'independent experts' to be identified as the lead authors. In addition, companies routinely cherry-pick from the available research data, publishing positive results and delaying or suppressing publication of the rest. On its own, this 'publication bias' leads to substantial overestimation of drug benefit and underestimation of harm.

Increasingly, in richer markets, the Big Pharmas are also accused of 'disease mongering' (Moynihan and Cassels 2005), and the lack of any control over the *volume* of product promotion is a relevant factor here. If not through 'direct-to-

consumer advertising’, companies typically buy into soft media and susceptible consumer groups, to provide all manner of ‘helpful’ information, supposedly to give patients more ‘choice’. Underpinning this marketing endeavour, the major companies routinely nominate, sponsor, and convene groups of selected professional ‘experts’ to develop statements of ‘best practices’ and treatment guidelines that have proved to have great influence in defining consumer ‘need’ and prescribing behaviour.

There is much more than this to be said – not least, substantial evidence of unfair attempts to neutralise or intimidate conscientious critics⁷ – but already the question is this. If we were all individually capable of knowing, synthesising, digesting, and processing all available (and obtainable) information on drug benefits and harms, would we not radically revise our views on the relationship between the two, and on where health value is to be found?

The question is rhetorical. The wider point is that – for all the progress seen, mainly in the highest-income countries – secrecy and non-disclosure still generally underpin commercial, professional, and governmental contributions to pharmaceutical endeavour. Lack of proper accountability remains the norm, and systematic and gross overestimation of therapeutic value for money is inevitably the result.

Response to health needs in developing countries

The present system of pharmaceutical endeavour inevitably falls far short of meeting basic health needs in developing countries. Pharmaceutical companies are market driven, by nature, design, and (company) law. They exist to develop and sell products to customers who can pay, and to trump competitors by any legal means.

The gulf between health provision and health need is underlined by the paucity of investment in R&D of drugs for the major neglected diseases. Between 1975 and 2004, only 21 out of 1,556 marketed new chemical entities were indicated for neglected diseases. This represents about 1 per cent of output, a figure unchanged in three decades (Chirac and Torreele 2006; Lexchin 2010). Médecins Sans Frontières (MSF) estimates that of the \$105 billion spent on medical innovation today, 90 per cent is spent on the health problems of less than 10 per cent of the world’s population (MSF 2006).

The underlying problem is acknowledged by some industry leaders:

We have no model which would [meet] the need for new drugs in a sustainable way ... You can’t expect for-profit organization[s] to do this on a large scale. If you want to establish a system where companies systematically invest in this kind of area, you need a different system. (Lexchin 2010)

Indeed, MSF suggests that some companies:

seem willing to explore new ways to be rewarded for their investments into

R&D ... At an MSF symposium on tuberculosis drug development in January 2007, representatives from several major pharmaceutical companies endorsed a statement supporting the UN talks aimed at producing a new R&D framework ... which would address the question of who pays for essential medical R&D, dissociating incentives from drug prices and rewarding innovation according to health care outcomes. (MSF 2007)

The key problem is to establish a system that, on the one hand, provides incentives to stimulate drug innovation in response to the greatest medical needs, and, on the other hand, provides access to affordable medicines. At present, these objectives seem quite incompatible, although various proposals have been made to reform the existing system over time. In the meantime, the main pressure point (and source of friction) relates to removing obstacles to accessing existing generic versions of useful drugs, thus saving millions of lives today rather than tomorrow.

While generic competition is critical to reducing drug prices and improving access to affordable medicines around the world, the patent system and other forms of intellectual property protection at present delay and obstruct the entry of generic medicines on to world markets. The patent system, globalised under the Agreement on Trade Related Intellectual Property Rights (TRIPS), is the dominant incentive framework for the development of new medicines, particularly where there is a profitable market.

Looking to the longer term, a number of proposals have been made for reforming the existing system of pharmaceutical endeavour, with a view to stimulating essential drug R&D and to delinking R&D costs from the price of medicines. Two model proposals are already in operation. But all of them have limitations, and also all face major obstacles, apart from a lack of resources. Seuba (2009) and Lexchin (2010) have identified the main barriers to expanding research capacity as follows: lack of effective prioritisation, coordination of research efforts, and capacity to conduct clinical trials in developing countries; failure to exploit publicly funded research; and stifling of initiative and free exchange of information resulting from the proliferation of intellectual property rights and patent thickets.

Public-private partnerships (PPPs), which exist in several different forms, are at present the most advanced of the various alternative models. They aim to integrate and coordinate industry and academic partners and contractors along the drug-development pipeline; to allocate philanthropic and public funds to appropriate R&D projects; and to manage neglected-disease R&D portfolios. A 2005 survey reported that 47 of 63 new drugs for neglected diseases were being developed under the auspices of a PPP. One-third of these 47 drugs came from PPPs involving Big Pharmas, the remainder from PPPs working with smaller companies (including some in developing countries) and from academic and public sector institutions (Moran et al. 2005).



41 Drugs in search of a disease (Indranil Mukherjee)

Another model, operational since 2008, is the US system of priority review vouchers.

Under this scheme, a company marketing a treatment for a neglected disease in the USA is entitled to a six-month review (instead of the standard 12 months) for any other product that it sells. This faster turnaround could reward a company with up to \$300 million by reducing the erosion of the product's patent life. While this model circumvents the usual obstacles of priority-setting and research coordination, Lexchin and others have suggested that it is otherwise of limited potential (Kesselheim 2008).

Other models to increase research capacity include an R&D treaty that will require governments to pay for essential medical innovation (MRDT 2005). Ambitious and detailed proposals have been made and also discussed at WHO,⁸ but obstacles have arisen and progress appears to be slow (Love 2009). Meanwhile, the main focus of attention is on prize funds. Different schemes have proposed a variety of payment mechanisms. What all these mechanisms have in common is that (potentially substantial) rewards for innovation are geared to the proven therapeutic value of a drug (Faunce and Nasu 2008; Love 2009; Stiglitz 2006; Love and Hubbard 2007). Although controversial, the prize fund mechanism *inter alia* is now acknowledged in the WHO Global Strategy Plan of Action as a viable mechanism for development.

It will be clear that the current challenges are formidable and that time is on no one's side. It remains to be seen whether, and to what extent, the leadership of pharmaceutical endeavour can rise to the occasion. In the meantime, the suffering continues on a breathtaking scale, not for want of technical solutions, as in the past, but for lack of political will.

Box D4 Medicines in search of a disease

In 2010 alone, drug companies paid US government agencies, insurance companies and patients more than \$2.7 billion in criminal and civil fines or settlements over their failure to fully disclose adverse drug effects or for illegal marketing of psychiatric drugs (making false claims about their safety or use).

Big Pharma-psychiatry's marketing to GPs and paediatricians has led to an enormous boost in the sales of psychiatric medicines. In 1989, an American Psychiatric Association (APA) 'Campaign Kit' told APA members, 'An increase of psychiatry's profile among non-psychiatric physicians can do nothing but good. And, for those who are bottom line oriented, the efforts you spend on building this profile have the potential to yield dividends through increased referrals' (American Psychiatric Association Campaign Kit 1989).

With the selling of mental illness to primary care physicians well in hand, the selling of psychiatric drugs follows. Harvard University psychiatrist Joseph Glenmullen, author of *Prozac Backlash*, writes, 'As they gain momentum, use of the drugs spreads beyond the confines of psychiatry and they are prescribed by general practitioners for everyday maladies' (Glenmullen 2000).

Today, through heavy marketing of its diagnoses and drugs, psychiatry no longer fights to emulate and gain acceptance from medicine; it has become an integral part of it. With that marketing, we've seen a dramatic increase in children being labelled with Attention Deficit Hyperactivity Disorder (ADHD), bipolar disorder and autism, thus creating 'false epidemics'.

Today, the US consumes 85 per cent of the international production of methylphenidate (Ritalin).⁹ The Council of Europe Parliamentary Assembly has also found high rates of methylphenidate consumption in Belgium, Germany, Iceland, Luxembourg, the Netherlands, Switzerland and the UK. In Britain, the stimulant prescription rate for children soared 9,200 per cent over an eight-year period, while in Australia there was a 34-fold increase in two decades (Johnston 2003). France reported a 600 per cent increase in the number of children labelled 'hyperactive' during the course of four years (Minde 1998). Sales of methylphenidate in Mexico have increased 800 per cent since 1993. In Spain, one of the largest exporters of methylphenidate, the consumption of this increases 8 per cent every year (Criado Alvarez and Romo Barrientos 1999).

'How can millions of children be taking a drug that is pharmacologically very similar to another drug, cocaine, that is not only considered

dangerous and addictive, but whose buying, selling, and using are also considered a criminal act?’ asks Richard DeGrandpre, professor of psychology and author of *Ritalin Nation* (Grandpre 1999: 177).

It has been argued that the source of ADHD and other mental disorders is a chemical imbalance that requires ‘medication’ in the same way that diabetes requires insulin treatment. This is false. In 2005, Dr Steven Sharfstein, APA president, admitted that there is ‘no clean cut lab test’ to determine a chemical imbalance in the brain.¹⁰ Dr Mark Graff, Chair of Public Affairs of the American Psychiatric Association, said that this theory was ‘probably drug industry derived’.¹¹

Notes

1 ‘Pharmageddon?’ www.socialaudit.org.uk/60700716.htm.

2 ‘Health care in the United States’. en.wikipedia.org/wiki/Health_care_in_the_United_States.

3 Since 1990, for example, the ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) has played an increasingly important role in defining the tests and standards used for approving drugs for general marketing. Its members comprise the European Commission, the US Food and Drug Administration, and the Japanese Ministry of Health, Labour and Welfare, together with the three associated trade associations – the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Japan Pharmaceutical Manufacturers Association (JPMA), and the Pharmaceutical Research and Manufacturers of America (PhRMA). At the same time, the Secretariat of the ICH is provided by the International Federation of Pharmaceutical Manufacturers’ Association (IFPMA).

4 ‘Pharmaceutical industry’. en.wikipedia.org/wiki/Pharmaceutical_industry;

5 See, for example, Starfield (2000); Perdomo (2010).

6 ‘Glaxo said to have paid \$1 billion over Paxil suits’. *Bloomberg Businessweek*, 20 July 2010. www.businessweek.com/news/2010-07-20/glaxo-said-to-have-paid-1-billion-over-paxil-suits.html.

7 For example, see David Healy

(psychiatrist), en.wikipedia.org/wiki/David_Healy_%28psychiatrist%29, and Nancy Fern Olivieri, en.wikipedia.org/wiki/Nancy_Olivieri.

8 Proposal by Bangladesh, Barbados, Bolivia and Suriname. Proposal for WHO discussions on a biomedical R&D treaty. www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_R_DTreaty.pdf.

9 ‘Evolution of the number of prescriptions of Ritalin (Methylphenidate) in the Canton of Neuchatel between 1996 and 2000’. Dr Jean-Blaise Montandon, Public Health Service, and Laurent Medioni, Chief of Pharmaceutical Control and Authorization Division, Switzerland.

10 *People* magazine, 11 July 2005.

11 Dr Mark Graff, interview, *CBS Studio 2*, July 2005.

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