

ATTENDING TO A SICK INDUSTRY?

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A Health Action International discussion paper

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Attending to a sick industry?

The value of medicines as part of the package of tools to promote health is uncontested. The place of medicines in the intervention against disease is subject of rather greater contention. As knowledge increases about the biology of disease, so too does the awareness that eradication depends on the appropriate use of, and the balance between social, environmental, and medical tools. But practices in health suggest that the balance is not being maintained. In rich countries, where infrastructure is good, health has been medicalised. So-called ›lifestyle drugs‹ promote the perception that for every ill there is a pill, whether or not other interventions, such as exercise and appropriate diet would be more suitable. In poor countries, a lack of adequate infrastructure is blamed for the absence of medicines to tackle pressing needs, especially where other interventions are insufficient or unsuitable. Neither rich nor poor countries are getting the medicines they need within comprehensive, balanced health systems.

Policy makers in rich and poor countries actively seek advances in technology and its application, believing these to be the best markers of, and tools for, advancement in society. Industrial policies reflect this: large investments are poured into biomedical science, for example. The call for technology transfer finds place in every international treaty, and indeed the right of citizens to benefit from science advancement is enshrined in the Universal Declaration of Human Rights, to which most countries are signatory. Every poor country without it yearns for local pharmaceutical production capacity, every rich country for the most advanced tertiary medical facilities. And the best country is the one which has or develops the best infrastructure and the most competitive industries for the production of the requisite goods.

But this urge to improve the lot of citizens the world over is being exploited by private actors to the detriment of public health. That high-tech is generally considered better than low-, is a perception

readily seized upon by astute marketers the world over. As a public, we are easily convinced of the merit of something new, be it only shiny or expensive enough.

Dazzled by all that is new, we are losing the ability to assess if new really is better than what we already have, or worth having at any cost. This applies in medicine as elsewhere. Not surprisingly, the more we invest in instituting industries whose existence depends on our uncritical reception of their products, the harder it will be to moderate the extents to which they will go to acquire our money. And the larger they grow, the more dependent we become, the greater their power of manipulation.

This power is being exercised without restraint. The crisis in innovation of medicines has been blamed by the pharmaceutical industry (and particularly the proprietary industry) on insufficient public investment, a claim uncritically accepted by many policy makers. Yet the industry is the most profitable in the world, and public investment in it has increased year on year for the last quarter century at least. This has not been matched by the production of new medicines to meet critical health needs. Indeed the priorities set by the industry show clearly that the motivation for medicines production is profit and not public health intervention.

It has long been debated whether or not the industry has moral or social responsibilities that derive from the nature of the goods it produces. That issue will not be revisited here. In fact it is secondary. What the industry does reflects the signals it receives and acts upon from public policy makers. If we want medicines to be produced to meet public health needs, then we must ensure that all our policies are geared towards this end. If public policy makers see public health first as an opportunity to increase competitiveness of their national or regional pharmaceutical industries, then it is only to be expected that the industry uses this as leverage in negotiations for ever more money for ever less useful goods.

The goods produced by the industry do not respond to the pressing public health needs of the day. This is a choice. The development of medicines relies on a complex set of interactions between basic research into the biology of disease, translational research in the clinical laboratory, and preclinical and clinical development of a medical product, which includes humans, safety and utility trials. Research leads to the design, characterisation, manufacture and refinement (development) and commercialisation of the medical product. Subsequent public uptake is a measure of the 'real life success' of the product, and post marketing surveillance of a medicine informs trans-lational research for future products.

But the choice of which medicines to pursue is part of a strategy of low risk and high profit. In the prevailing system, research is heavily dependent on development and sales. It is funded by the success of commercialisation, with the consequence that the approximation of the potential for commercialisation will influence choices made about what future medicines to produce. The desire of pharmaceutical companies to produce ›blockbuster‹ medicines and their far greater investment in sales and marketing than in research and development are manifestations of the low risk, high profit strategy. This may be good for company ledgers but has stark consequences for the public.

The strategy of pursuing diseases of the rich has the direct consequence that the diseases of the poor, even where basic biology is well known, are ignored. Over time the neglect of the diseases of the poor extends from availability of medicines back to investment in translational research. The poor public in poor countries are deliberately left to die, because blockbuster profits cannot be envisioned from treating what ails them.

But the rich are not necessarily better off. Where the numbers of people who suffer from a disease are small, even if they are rich, the strategy means that the industry declines intervention. Such is the case with many orphan diseases.

Pricing at 'what the market will bear' means that rich people are sold medicines on the back of heavy marketing for those diseases from which they suffer whose biology is well understood¹. Similarly for those diseases where biology is moderately well understood, and people moderately well off, development of products depends on aggressive marketing, and on the potential for broad spectrum use of the medicines for diseases categories, such as depressive disorders. The emphasis on return on investment from the private sector is directly responsible for the distortionary policies now seen in medicines' production.

Policy makers choose to address the consequences of pharmaceutical strategy by offering a variety of incentives for industry to take the risk of producing medicines that correspond to public health needs. Tax credits and exemptions, research grants, intellectual property protection are some of the measures used to try and stimulate innovation.

The response of the industry has been to demand ever more incentives from the public. Extraordinary expense is now associated with medicines production. This despite the scant evidence that monies previously invested have diverted companies from their chosen strategy. The question must be asked why governments continue to seek solutions in a failing model of medicines' research and development.

The perverse consequence of reluctance of governments to acknowledge the failure of this model has been a marked increase in the dishonest behaviour of industry. Whereas in the past industry may have simply refused to take on high risk research, in recent times a number of scandals have emerged that implicate industry in actively distorting science and medicines production in order to maximise profits from those medicines they choose to pursue, or maximally exploit tax and other incentives.

The corruption extends from basic research to post marketing surveillance. Evidence capture, documented manipulation of research data² to support the advancement of a given medical product of

questionable value, and to steer it through the regulatory process onto the market begins with the payment of scientists to conduct research that shows the value of a product being sponsored by a given company. At the same time, ›evidence‹ of the existence and severity of a medical condition or class of disorders is promulgated through the academic community by the same or other scientists, typically through symposia. Papers are published in academic journals which disclose only favourable data about the product being promoted. Sometimes these are ghost-written by people paid by the industry, and scientists are paid to put their names to papers they have never seen³. Evidence capture occurs both in basic and clinical research. Medical journals are aware of the problem, but are constrained in their ability to act to tackle them.

That this practice is unethical is not in question. It is also dangerous – regulators rely on data from studies to assess the safety and therapeutic value of medicines. Media exposure has revealed that industry actively suppresses unfavourable data. But even if this were not the case, the absence of complete data to make analyses of new products corrupts any decisions that are made from partially complete dossiers.

Capture of science also occurs through the financing of research centres at universities – typically universities of standing – to work on issues in which industry is interested. This has the dual effect of lending perhaps undue credibility to any work subsequently undertaken, and of limiting the type of open research possible at universities, where attraction of funding is a key to advancement. Universities lose their place in society as generators and disseminators of knowledge free of influence⁴. When they then enter into intellectual property agreements with sponsor companies, they, wittingly or otherwise, limit the availability of knowledge to other scientists, and impede the advancement of science. Increasingly the relationships between universities and the pharmaceutical industry raise questions about the availability of information for basic or applied scientific research.⁵

The capture of academic research has the additional consequence of influencing the funding priorities of public authorities, who use the literature as a guide on what research areas deserve priority. Tainted data made available to regulators makes difficult their task in an environment where pressure exists not to impede the process to market of products that make national or regional industries competitive with each other. The problem is recognised.

The expense involved in developing and adhering to standards for drug evaluation is high, and has been identified by some as the primary obstruction to innovation. The suggestion is that by limiting the expense of such standards (by reducing the number of tests or by lowering the safety standard) innovation could be spurred.

From the public perspective the solution is not to increase profits at the expense of safety, a sentiment shared by regulators: »because safety issues are a significant cause of delay and failure during development, some have advocated simply lowering safety standards. This is not a preferable solution. For ethical human testing, there is wide agreement that reasonable assurance of safety must be assured before clinical trials begin. Patients, prescribers, payers and the public share the expectation that marketed medical products will have a well-understood safety profile and a positive benefit/risk analysis«⁶

Unfortunately, the capacity of regulators to apply this sentiment is in question. Regulators themselves are not free of the influence of industry. Regulatory capture occurs because regulators are funded by the products of the industries whose products they assess⁷. This industry also finances their political paymasters⁸. The failure of regulators to address the evidence of the dangers of Seroxat in the UK and Vioxx in the USA are illustrations of the reluctance of regulators to challenge a powerful authority⁹. Evidence of corruption of regulation has emerged in both countries. The use of external regulators with links to, or indeed in the pay of companies whose products were under review has caused public outcry and prompted examination of the relationship between regulators and the pharmaceutical indus-

try. The US House subcommittee on oversight and investigations has strongly criticised the National Institutes of Health (NIH) ethics policy as »encourag[ing] the option of corruption.«¹⁰

The influence of industry over policy makers even where there is no direct evidence of corruption is a cause for concern. The access of industry to high level decision makers is linked to the desire of countries to compete on the global stage. Public consultations on the direction and stimulation of innovation rarely include the public. In fact they are more typically consultation with industry in various guises. In the recent consultations of the European Agency for the Evaluation of Medicinal Products¹¹ on its framework programme to 2010 involved consultations with 10 companies, to be expected, but also with eight patient and consumer groups, six of which are directly funded by the pharmaceutical industry. Recent consultations of the Directorate General for Research at the European Commission included only patient groups directly funded by industry. Regulators must have public perspectives if their decisions are truly intended for the public.

The corruption of research and regulation is if anything outdone by the extent to which medicines are misleadingly promoted to doctors, nurses and other prescribers and to the public. By far the largest investments in medicines are made in marketing and advertising. Direct to consumer advertising, drug information and drug awareness campaigns are aggressive strategies ostensibly in the interest of the patient to increase market share of companies for their products. It involves the establishment or purchase of patient groups to influence policy makers and public opinion, the use of celebrities to promote medicines through established media programmes, partnerships with hospitals, placement of nurses in health facilities, inducements to doctors, or medical students¹², and the tried and tested use of sales representatives to knowingly misrepresent the value and application of medicines to prescribers¹³.

This corruption of medicine is intentional, and it is inevitable, in a system where the value of a medicine is in the stock of the company that produces it, where shareholders want ever increasing returns, and where the personal gain accruing to decisionmakers is derived from the pleasure of shareholders. Where scientists, regulators and policy makers are in the pay of or subject to coercion by a very powerful actor, it is perhaps to be expected that the unseen public is also unheard. Science is no longer a driver of medicines production. Public safety is at best a conditional second.

The deeper consequence for the public – apart from the financial costs they have to bear for medicines they may not need – is uncertainty about the safety, value and effectiveness of the medicines they consume. They do not, and cannot know if every time they take a pill, or participate in a research trial, they are endangering their lives, because every level of the medicines production system has been corrupted. They cannot be sure that anyone is acting in their interest.

From basic research to marketing of medicines what is needed is rationality in drug policy. Laxity in oversight of the pharmaceutical industry has allowed the institution of policies that corrupt medicines production, bankrupt public health systems, and jeopardise the public's health.

Corruption will continue unless governments intervene to reward innovation of medicines by means other than the aggressive commercialisation of medical products. Remedy can only be found in the correct diagnosis. Governments can no longer continue to pre-occupy themselves with symptomatic approaches to the crisis in innovation. By linking profit making in pharmaceuticals with the granting of monopoly rights, governments institute the dangers of dishonest representation of the value of products. They raise the incentives for the industry to actively seek to influence the regulators and uses of medicines.

Health Action International recommends that governments undertake a serious and systematic review of alternative models of financing research, in particular to break the link between the conduct of science and commercial interest. The basis on which the current system is rationalised needs to be backed by evidence. The choice of policy makers to accept the current systems means abuse of all of the public, whether through over-medicalisation or neglect of their disease.

Public funds invested in basic research must carry the condition that the proceeds of this research be available to the public. The public must have access to what they pay for. The relationship between researchers and their sponsors must be made transparent to end the contamination of scientific literature.

Regulators and doctors must be freed from the influence of medicines producers, to allow their judgements about the suitability and safety of medicines to remain free from prejudice. Pharmaceutical data from clinical trials needs to be made publicly available, in a manner that allows public interpretation of results.

Information to the public and patients about new pharmaceutical products must be provided from independent sources. Post-marketing surveillance of medicines must be established in such a manner as to assure that patient reports about their experience of medicines are not ignored or distorted by doctors, regulators or producers of medicines.

Policy makers in research, regulation and financing of health need to make active efforts to assure that they know with whom they are dealing in their consultations, and to open their processes to the public.

Finally those investing public money must make clear where the money has gone and what the outcomes of the investment have been. The European Investment Bank has a role to play in this regard.

Policy makers, even the best intentioned of them, cannot know if they are making reasonable decisions about the allocation of public resources if they are not aware of the biases of those with whom they consult. It is not enough to conduct technical exercises that on the surface are directed at the public if the evidence is contaminated. If governments choose to continue to adopt a symptomatic approach to regulation of the pharmaceutical industry, the result will be the same as it has been for the last quarter century. Ever more money will be demanded from an industry that will become ever more opaque. Deceit will become ever further engrained in industrial practice. Opacity will accompany it. It will matter little whether governments try to direct badly needed research. Priorities set using distorted data, are distorted priorities, and no amount of money will disguise the fact.

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- 6 US Food and Drug Administration: Stagnation or Innovation: Challenge and Opportunity on the Critical Path to New Medicines; March 2004; from: www.fda.gov
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- 11 The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future; March 23, 2000; Doc ref: EMEA/H/34163/03/Rev2.012
- 12 See www.haiweb.org, www.drugpromo.info, www.nofreelunch.com, or www.healthyskepticism.com for detailed bibliographies
- 13 Kaiser et al: Sind die Aussagen Medizinischer Werbeprospekte Korrekt? [Are the claims of medical information advertisements true?]; Arznei-Telegramm; February 2004

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