



A HEALTHY MARKET?

Pharmaceuticals, incentives
and innovation

A Healthy Market? Pharmaceuticals, Incentives and Innovation

By Jacob Arfwedson

This brief paper will state the case for a market in medicines, based on three hypotheses:

- Medicines are a product to be treated like any other good.
- As a product, medicines need to be subject to market conditions.
- The high and rising cost of medicines is to a large extent caused by the lack of market mechanisms, rather than their pervasiveness.

This approach may seem obvious, but it remains anathema to many, if not most of the participants in the policy debate on healthcare reform. The reasons are many and partly overlapping, but may be summarised as follows:

- The production, distribution and sale of pharmaceuticals is intimately linked to the healthcare system, the bulk of which remains controlled and financed by government in developed countries.
- Medicines are part and parcel of the welfare state policies which have elevated healthcare into an intricate system of positive 'rights', subject to political control, rather than to consumer choice and demand.
- The free market is believed essentially incapable of producing equitable access to healthcare services. Therefore government must ensure redistribution and price controls on medicines.
- In recent years, the very foundation of industrial innovation based on intellectual property protection has come under heavy fire, introducing the ideas of producing medicines on open source premises, or even reverting to Soviet-style prizes.
- Paradoxically, the very market forces which supply new medicines are attacked, because innovative products are not immediately available to all

By looking at the nature of innovation and entrepreneurship which form the basis of genuine progress, be it for medicines or other products, this paper will form a counter argument to the dominant discourse as outlined above.

Medicines and innovation

For my part, I consider that medicines are one of the greatest blessings in our time – perhaps the greatest.

Ernst Chain, discoverer of the medical use of penicillin

We sometimes tend to forget, or take for granted, the enormous scientific developments and industrial achievements that have taken place over the past century, in medicine as well as in other areas. My grandfather, although by no means lacking materially, almost died of polio in the 1920s; my daughter, had she been born in those days, would likely have succumbed to persistent middle-ear infections as a baby. Seventy years later, my daughter can get the right antibiotics within an hour of seeing a doctor.

Our perception of well-being may be best evaluated, not in terms of what we do have, but what we would and could have tomorrow. This basic observation of human behaviour should be remembered when discussing producer innovation and consumer needs.

The prerequisites of innovation are well established, but need to be restated, since the basic institutions of free markets, intellectual property protection and rule of law are increasingly under attack.

The pharmaceutical sector in the EU represents 17% of the business research and development expenditure and approx. 3.5% of the manufacturing added value (2005).¹ Yet newspaper headlines have for several years highlighted the lack of new medicines, despite high industry earnings and profits. This has cast doubts on the real value of the tacit agreement which underlies the public/private partnership between government and industry: the former will tolerate and support the trade-off between investments and profits as long as the latter delivers new goods. Since there has been disturbing evidence that innovation is faltering, politicians and NGOs have been intimating that the deal should

¹ EFPIA 2005.

be reconsidered (e.g. through higher or special taxes on companies and compulsory licensing of medicines for poor countries).

Emerging markets: friend or foe?

The US and EU share of the world market in medicines is declining, from respectively 58% and 26% (2001) to 34% and 19% (2005) as global consumption keeps rising. According to IMS Health, worldwide sales increased by 7% in 2005 to attain \$602 bn. Market growth is expected to remain at this level for the next decade.²

It is (...) quite wrong to say, as so many economists do, that capitalist enterprise was one, and technological progress a second, distinct factor in the observed development of output; they were essentially one and the same thing or (...) the former was the propelling force of the latter.

Joseph Schumpeter, **Capitalism, Socialism and Democracy** (1942)

The keyword is innovation, but it is rarely defined. Critics tend to consider that the absence of breakthroughs should be regarded as the failure of either markets or of industry. But although 'innovative' is a basic requirement for patent approval of new products, this quality is not a question of either/or. Indeed, we would be grateful to welcome the equivalent of penicillin every six months; in reality, research rarely evolves in this regular fashion, but rather by fits and starts like most entrepreneurial activities.

It remains true nevertheless that new products against high blood pressure and cholesterol have contributed to reducing mortality due to cardiovascular diseases. Vaccines have practically eliminated polio, measles or diphtheria. Anti-depressants have helped to drastically reduce suicide rates in many countries.

Beauty is in the eye of the beholder; innovation may often be a matter of consumer preference and comes in many flavours. Innovation, for medicines as for other products, ultimately lies in the hands of the individual. Specifically, innovation in medicines may pertain to second or third generation products avoiding previous allergies and side-effects, or the combination with other medicines. New products have led to a reduction or elimination of surgery and costly hospital stays, e.g. for ulcers today or tuberculosis historically.³ Too little attention is given to the positive trade-offs whereby new medications can replace existing therapies, helping to reduce overall health costs.

An often ignored aspect of research is serendipity, i.e. positive but fortuitous results of research projects which initially were heading elsewhere. Historical examples include the use of aspirin for patients having suffered a heart attack; more recently the product Evista, initially approved for bone mass issues in female patients (osteoporosis) has since proved to be a very potent remedy against breast cancer.⁴

But striking gold while digging for iron ore belongs to the area of independent research through trial and error essential for every scientific venture. However desirable, these are outcomes which no single individual, politician or public administration may reasonably plan for, or mandate by law.

In recent years, critics have argued that the trade-off between patent protection and delivery of new products should be reconsidered, as the pipeline seemed to be drying up. In reality, there are many encouraging signs, in particular in the field of biotechnology and pharmacogenomics.⁵ In 2005, the sector exceeded revenues of \$60 bn for the first time, R&D expenditure rose by 15% and the number of products increased by 38%.⁶ In the US, the greatest motor for this development were cancer drugs from the California laboratories of Amgen and Genentech which now represent 13% of US sales.⁷

These efforts also largely correspond to patient demands, in particular in Europe: according to a poll in 11 EU countries, close to 70% of patient respondents said that increasing the number of medicines or treatments available would be 'likely or very likely' to increase the quality of their country's healthcare.⁸

² *Le Figaro Economie*, 22 April 2006.

³ Cf. F. Lichtenberg, 'Benefits and Costs of Newer Drugs', NBER Working Paper, 2002.

⁴ A product developed by Eli Lilly.

⁵ Cf. 'Biotechnology and Tailor-Made Medicines', Amigo Society/Stockholm Network, Brussels February 2006.

⁶ *Pharma Marketletter*, 17 April 2006.

⁷ *Les Echos*, 24 February 2006.

⁸ **Impatient for Change; Poles Apart** (Stockholm Network/Populus: London, 2005, 2006)

Conditions and obstacles to market provision

Having examined the benefits of market dynamics for innovation, let us look at the forces constraining these institutions.

Costs and benefits of regulation

In Europe, the US market is frequently held up as an example of an unfettered market with few regulations, leading to serious incidents involving inadequate or dangerous products. In fact, pharmaceutical markets on both sides of the Atlantic remain the most strictly regulated industries in the world. To appraise the call for more stringent rules, following the recent withdrawals of medicines⁹ from the market, it is necessary to backtrack a couple of decades.

During the 1960s, regulatory policies in the USA became more severe than regulations in the United Kingdom. A 1976 study¹⁰ shows that the impact of the US regulations significantly delayed the arrival of new drugs on the market: from 1950 to 1961, the number of new drugs on the American market was on average 56 per year; between 1962 and 1976 it had fallen to 17 per year. Studies also found that this reduction was much greater in the USA than in the UK, France or West Germany during the same period.

Another study¹¹ examined the effect of the new regulations on research opportunities in the USA and the UK. The authors assumed that factors unrelated to regulation would reduce the research intensity in both countries, but that for reasons linked to regulation this reduction would be greater in the USA. The results showed that between 1960-61 and 1966-70 research productivity dropped six-fold as compared to three-fold in UK. The study also confirmed that the concomitant decline in profitability induced US pharmaceutical companies to relocate their research abroad. The percentage of total research investments overseas increased from 9.9% in 1972 to 15.4% in 1974.¹²

Today, the situation is the reverse: research is still done by Europeans, but increasingly in the United States, or elsewhere. Between 1990 and 2004, investment in research increased almost twice as fast in the US compared to Europe; at the same time, emerging markets such as China and India are catching up.¹³

The price of precaution

To what extent should we refrain from risk-taking in order to attain greater safety? Answer: it is the wrong question. Human existence, including innovation, is fraught with dangers. Indeed, the very search for safety implies taking risks, i.e. safety and risk-taking are two sides of the same coin. If we accept this, the concept of 'zero risk' is clearly non-sensical. The challenge is instead to make risk-taking, through innovation, conducive to safety.

For those who think of safety as an absolute, things are simple: regulatory policies should take action towards this goal. If on the other hand we posit that safety is relative, and something that must be continually discovered and improved, the situation is quite different and results in two diametrically opposed strategies: trial-and-error versus 'no trial without prior guarantee against error'.¹⁴ Or in current terminology, the precautionary principle.

It is true that no trial means no error, and therefore no risk, at least superficially (this is the strategy adopted, for instance, by the French government when 'governing'.) But the absence of errors also means that there will be less information about what works and what doesn't: less knowledge will be accumulated as a result.

A recent example in policy involves genetically modified organisms and biotechnology in general. It may seem prudent, *a priori*, to restrain or control development of new products as long as their potential negative impact is unknown. But this also implies that regulators can know, *ex ante*, how to separate beneficial from negative risks. In the case of GMOs, not a single case of poisoning or other serious incidents has been reported since the practice began. Yet precautionary policies have gained the upper hand; better safe than sorry. This is what you see. What you don't see are the millions of people in Africa and Asia who could be (and are in many places) saved from starvation by using GMOs.

⁹ Cf. Vioxx and Bextra were withdrawn in 2004 and 2005.

⁵ Grabowski et al, cited in Gudmundsson, p. 202

¹¹ Grabowski, Vernon and Lacy. 'Estimating the Effects of Regulation on Innovation: An International Comparative Analysis of the Pharmaceutical Industry', *Journal of Law And Economics*, April 1978. Cited by Gudmundsson, p. 203.

¹² *Idem*, p. 203.

¹³ EFPIA, 2005, p. 2.

¹⁴ This concept stems from Aaron Wildavsky, 'Searching for Safety', Transaction Books 1988

Regulations are also a major driver of both human and monetary costs. The costs and benefits of the development of new medicines are germane when considering an optimal equilibrium between the incentives granted to innovative companies and the simultaneously urgent needs of speedy approval of new medicines and legitimate safety concerns. However, the incentives governing regulators and inventors are very different. The former risk dismissal by their superiors, and potentially even criminal action, if a medicine is approved and subsequently proves damaging ('Type I error'); but they will receive none of the benefits from a rapid approval of a new medicine. The costs of delays in the regulatory pipeline on the other hand are borne by industry, and ultimately by consumers ('Type II error').

The length of the FDA approval process for new medicines has doubled since the 1960s; the financial costs have doubled since the late 1980s. Moreover, the number of clinical trials for each new product doubled from 1977 to 1995, and the number of patients involved tripled.¹⁵ According to a 2004 study, the net social cost of healthcare regulations amount to \$169 bn. We may compare this to the amount spent in 2002 by Americans on petrol and oil (\$165.8 bn) or on pharmaceuticals (\$162.4 bn).¹⁶

In Europe, the recommended deadline of 180 days of patient access to new medicines sometimes amounts to 450 days. In fact, a 2005 report has shown that 'in 20 out of 25 EU countries, between 15-48% of medicines licensed in the last five years were unavailable'.¹⁷

What price innovation?

This brings us to the highly sensitive issue of pricing of medicines. Several arguments are involved.

First, new medicines are sold at a premium corresponding to their merits compared to older counterparts. This raises criticism on two contradictory levels. For a start, it is considered that new products are not that new (see above) and that higher prices have no justification in terms of therapeutic benefits. Second, it is contended that innovative medicines should be accessible to all, at once. Curiously, these arguments are sometimes advanced concurrently.

As we have already seen, pharmaceutical prices are not subject to market mechanisms, quite on the contrary in fact.¹⁸ Although these represent a fraction of overall healthcare costs (on average 10%), it remains the visible part of the iceberg for which the level of pricing is debated by public officials and the media. Producers of medicine have to deal with public officials and politicians to get their products approved for reimbursement within the government healthcare system in each country. This is the outcome of a political process; and again, this is what you see.¹⁹

What you don't see is the volume of overall health costs, which remain opaque, both to patients and to providers. Hence the difficulty in evaluating the performance of healthcare systems worldwide. The price of medicine becomes a target for polemics, because it is relatively visible; remaining costs are largely outside of any market mechanism to the detriment of all parties. This is why producers of medicine are sometimes accused of being subsidised by the public health systems: 'costs are socialised, profits privatised'. This reflects the monopsony power of government buyers in the EU market, as underlined by a recent study.²⁰ On the other hand, it has been shown that the larger the proportion of pharmaceutical sales are subject to price controls, the smaller its R&D expenditure will be as a proportion of its sales.²¹

As somebody has said, 'the rich are the guinea pigs who try out high-cost products of lower quality, so that the rest of us may later enjoy high quality, low cost products'. This applies to medicines as well. Put differently, 'first-in-class medicine should not be assumed to be the best-in-class'.²² Decentralised trial-and-error occurs every day in the market by millions of individuals creating new products, discarding them, inventing new ones and improving older ideas. The more numerous these activities become, the more information will be accumulated, gainful risk-taking will be rewarded and those which are not will be avoided, competition is intensified and prices are continuously pushed downwards. We may observe the benefits of competition in the generics market, where medicines are substantially cheaper in the US than in the EU, mainly because of market size (5-6% in EU of the market vs. close to 50% of prescriptions in the US) and greater competition in the former.

¹⁵ Cannon and Tanner, p. 121.

¹⁶ *Idem*, p. 112.

¹⁷ IMS Global Consulting, cited by EFPIA, p. 4.

¹⁸ For a detailed analysis, cf. 'The Human Cost of Pharmaceutical Price Controls in Europe: the Case for Reform', Centre for the New Europe, Brussels 2004. (http://www.cne.org/pub_pdf/2004_07_01_humancost.pdf)

¹⁹ Cf. the introduction of reference pricing and compulsory generic substitution to reduce expenditure in the EU.

²⁰ Calfee et al (AEI-Brookings 2006)

²¹ J. Vernon, Wharton School, quoted in Bandow, p. 15.

²² OHE study, p. 27.

Contrary to popular belief however, the US system is highly socialised and should not be used as an example of market-based healthcare. However, price competition is considerably more developed in the US for follow-on medicine than in other countries. Studies have shown that a majority of new products are marketed at discounts, both compared to the highest price in a class of medicines and to the class average price. This is the case also in a few European countries (e.g. Germany and the UK) where the so-called 'me-too' products enter the market at a lower price than the first medicine. Conversely, the benefits of price competition are low or nil in countries with more stringent price controls.²³

Market access depends both on the intellectual property regime and pricing systems. But whereas the structure of the patent regime may vary according to a country's wealth and level of development, it remains true that price controls slows innovation and delays market entry of new products.²⁴

Conclusion

It is high time to establish objective measurements of healthcare systems in terms of consumer benefits of output. Only when this starts to happen will there be an embryonic standard by which the benefits of market reform may be genuinely gauged. Only when true costs assumed by the taxpayer and future consumer of health services are transparent, will the relative cost of medicines be appropriately evaluated. And finally, this means that when eventually political decision-making yields to consumer concerns in terms of market reform, we will see real benefits. This may seem chimerical, but the reality of cash-strapped public systems will eventually move us closer to this goal.

As a former Canadian Health Minister once stated, 'We know what goes in, but we know too little about what happens with the huge amount of resources spent.'²⁵

Finally, I would like to reflect on the title of this series. In order to establish a healthy market for pharmaceuticals, we need a new approach: innovation and progress come from innovators, not from government. Although regulation for medicines is legitimate and necessary, the evidence of recent years shows clearly that government intervention regularly prevents entrepreneurial action from flourishing, resulting in limited competition, either through reference pricing and price controls, or through wasteful regulations in terms of product approval.

A competitive market for medicines is possible, provided that government action restricts itself to implementing safety standards which allow for speedy market entry of new products, even if this means taking additional risks (e.g. authorising the use of experimental drugs for the chronically ill or terminal-stage patients).

As has been shown, the increasing price of medicine can often be traced to overbearing regulations and restrictions on market access. There is no persuasive evidence that these avatars are the product of proper market processes, on the contrary. The decline in clinical trials in developed nations for cost reasons clearly indicate the way forward in policy terms: only a regulatory approach set on facilitating research and an acceleration of marketing approval will prove conducive to overall health outcomes.

The globalisation of markets confirms this trend; research and innovation will always occur, and patients will move to satisfy their needs. Therefore, the competition among national regulatory environments will increasingly determine the final outcome.

Market dynamic, as opposed to regulatory peristaltics, are essential to wealth creation which is the fundamental condition for healthy economics, and by implication health economics. The scale is boundless; the basic principles are inherent in human action.

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²³ OHE study, p. 26-27.

²⁴ Cf. Lanjouw (NBER, 2005)

²⁵ OECD Health Ministerial Meeting 2002.

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