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Is it possible to have cheaper drugs and preserve the incentive to innovate? The benefits of privatizing the drug approval process

Corinne Sauer · Robert M. Sauer

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Abstract In this paper, we argue that lower prices for pharmaceuticals can be achieved by fostering a new type of competition in the pharmaceutical industry. Lower drug development costs, and hence prices, can be brought about by abolishing national drug administrations and replacing them with private certification boards that compete on the basis of safety, efficiency and cost of their drug approval process. A major benefit of this type of privatization is that it would not necessitate limits on data exclusivity in order to achieve lower prices. Drug approval privatization could achieve the same positive results as generic competition, in terms of lower costs and prices, without the negative effects of intellectual property rights violation and the consequent discouragement of innovative activities.

Keywords Pharmaceuticals · Drug approval · Privatization · Data exclusivity · Innovation

JEL Classifications D42 · D73 · D92

> ''The FDA has done enormous harm to the health of the American public by greatly increasing the costs of pharmaceutical research, thereby reducing the supply of new and effective drugs, and by delaying the approval of such drugs as survive the tortuous FDA process.''—Milton Friedman.

C. Sauer
Jerusalem Institute for Market Studies, Covshei Katamon 26/3, Jerusalem, Israel
e-mail: corinne.sauer@jims-israel.org

R. M. Sauer (✉)
Division of Economics, University of Southampton, Southampton SO17 1BJ, UK
e-mail: r.m.sauer@soton.ac.uk

1 Introduction

The price of pharmaceuticals is an issue of great concern for governments around the world. Soaring national health budgets and the fear that underprivileged populations have only limited access to life-saving medicines, has motivated policymakers to seek ways in which they can intervene in the market for pharmaceuticals. The most widespread solution that governments have adopted for affecting the price of pharmaceuticals is to foster generic competition. National regulatory authorities currently allow potential entrants (generic firms) to use test data, generated and paid for by already existing innovator firms, in order to gain marketing authorization for their competing products. Generic firms need only show bio-equivalence. They do not need to incur the same level of costs as the innovator in performing clinical trials. The ability of generic firms to ''free-ride'' on the investment of innovators enables them to charge lower prices upon expiration of the innovator's period of data exclusivity.

Generic competition has so far been quite successful in achieving the intended goal of lower drug prices. However, government-sanctioned ''free-riding'' also has its drawbacks. Although prices in the market for pharmaceuticals have come down, the development costs that research-based pharmaceutical companies incur have not. This harms the incentives for innovators to continue innovating. Policymakers are essentially gambling that the very visible benefit of lower current prices for existing pharmaceuticals will outweigh the much less-visible social cost of future life-saving drugs never being introduced to the market.

This paper argues that lower prices for pharmaceuticals can be achieved by fostering a different type of competition in the pharmaceutical industry. Generic competition should not be thought of as the only way to foster competition and reduce prices. Lower drug development costs, and hence prices, can also be brought about through a privatization of the drug approval process. National drug administrations could be abolished and replaced with private certification boards that compete on the basis of safety, efficiency and cost of their drug approval process. A major advantage of this type of privatization is that it would not necessitate limits on data exclusivity in order to achieve lower prices. That is, drug approval privatization could achieve the same positive results as generic competition, in terms of lower costs and prices, without the negative effects of intellectual property rights confiscation and the consequent discouragement of innovative activities.

The rest of this paper unfolds as follows. The next section reviews the empirical evidence that suggests that intellectual property protection (such as data exclusivity) is important for continued innovation in the pharmaceutical industry. Section 3 describes the different systems of intellectual property protection currently in place in the US and Europe, and the origin of generic drug competition. Section 4 focuses on the accelerating costs of the current monopolistic regulatory drug approval process. Section 5 expands upon the main idea of the paper, the feasibility and desirability of an alternative competitive market in drug certification. Section 6 summarizes and concludes.

2 Intellectual property, profits and innovation

New drugs are the fruit of long and costly research and development (R&D) by pharmaceutical companies.[1] R&D investment by pharmaceutical companies amounted to more than $60 billion in 2003 in the U.S and in Europe. One of the most important factors that

[1] The Association of the Pharmaceutical Research and Manufacturers of America (PhRMA) reported an estimated $33.2 billion on R&D expenditures in 2003. The European Federation of Pharmaceutical Industries and Associations (EFPIA) reported R&D investment of 21.1 billion euros for the same year.

supports continued investment in R&D is intellectual property protection. A well-known study by Mansfield (1994) arrived at this conclusion by surveying the R&D directors of 100 U.S. firms between the years 1981 and 1983. Respondents were asked to estimate the fraction of their inventions that would not have been developed without patent protection. The average fraction across all industries was 14%, while in the pharmaceutical industry it was 60% (see also Levin et al. 1987; Cohen et al. 1997). Taylor and Silberston (1973) found similar results in a survey of U.K. R&D-doing firms. The data indicated that in the absence of patent protection, R&D investment would have been 64% lower.

These pioneering studies of the role of intellectual property rights (IPRs) in R&D activities, have raised the question, why are IPRs so much more important in the pharmaceutical industry than elsewhere? Grabowski (2002) provides a compelling answer. He argues that IPRs are crucial in pharmaceutical innovation because of the high cost of innovation relative to the cost of imitation. Patent protection and data protection provide innovators with a period of market exclusivity that allows them to recoup their large initial investments and earn a profit. Without such protection, innovative products would be quickly imitated at a very low cost, rendering the original R&D effort almost worthless.[2]

On a related point, Grabowski and Vernon (2000) find that among the 118 new chemical entities (NCEs) introduced to the market between 1990 and 1994, only 30% of them had a present value of net revenue that exceeded their R&D costs. For the median drug, the cost of R&D was not recovered. It was only among the few high selling drugs, known as blockbusters, that the return to R&D was substantial (five times greater than the return to all other drugs). This wide range of returns in new drug investment led the authors to conclude that R&D effort in the pharmaceutical industry is mainly driven by the search for a blockbuster.

In fact, research-based pharmaceutical companies need to have some top selling drugs in order to cross-subsidize other less-profitable R&D investments. Legislative enactments that weaken IPRs and lower the price of blockbusters, without lowering costs of development, could therefore cause a cascading reduction in pharmaceutical innovation. Giaccotto et al. (2003) provide empirical evidence for this latter contention, in the context of price controls. They find that pharmaceutical R&D would be 30% lower were the U.S government to introduce price limits on drugs. Lowering R&D by 30% would result in 330 to 365 fewer new drugs within a 20-year period.

On the issue of pharmaceutical price controls, Brouwers et al. (2004) similarly find that if countries imposing price controls were to remove them, R&D expenditures would increase by $17 to 22 billion, and between 10 and 13 new compounds a year would be introduced to the market. In a recent paper by Acemoglu and Linn (2004), it is found that a 1% increase in market size for a drug category would lead to a 4–6% percent increase in the in the number of new drugs brought to the market.

The accumulated body of empirical evidence thus makes it quite clear that price controls and weak IPRs discourage R&D expenditures and innovation.[3] Nonetheless, it is still legitimate to ask just how costly less innovation is to current and future generations. That

[2] In general, firms that produce easily copyable goods, like pharmaceuticals, chemicals, and software are more concerned with IPRs than firms investing in products that are costly or difficult to imitate, like computer hardware or electronic assembly equipment (see Levin et al. 1987).

[3] The link between IPRs, innovation and economic growth is exhaustively examined in Lerner (2002), where it is found that relatively wealthier countries are more likely to have patent systems, to grant longer patents, and to respect other countries' patent rules. See Hassett and Hubbard (2002) for a review of the literature that links profit variables with the level of business fixed investment (such as R&D). See also Griliches (1992) for the importance of R&D investments in explaining economic growth throughout the 20th century.

is, lower prices for already existing drugs that follows from generic entry, and which are brought about by the violation of IPRs in the form of weak data protection, could potentially outweigh the social costs of less pharmaceutical innovation in the future.

On the benefit side of the equation, The U.S. Congressional Budget Office (CBO) (1998) found that consumers save a substantial amount of money. Consumers of pharmaceuticals saved between 8 and 10 billion dollars from 1990 to 1995 due to price competition from the generic industry. At introduction, generics sell, on average, at 61% of the brand name. After 2 years, as more generics enter the market, generics sell, on average, at 37% of the original brand name (see Grabowski and Vernon 2000).

On the cost side, the CBO study also found that the U.S. Hatch-Waxman Act, which further eased the entry of generics into the drug market, had a significant negative impact on R&D by research-based pharmaceutical companies. A study by Lichtenberg (2002) provides more direct evidence on the social value of innovation in the pharmaceutical industry and the potential loss to society of less R&D activities. He finds that pharmaceutical R&D and the introduction of new drugs significantly impact the economy through increased longevity, productivity and savings in other types of medical expenses. New drug approval in a given year increases the lifetime expectancy of people born that year by .016 years. Aggregating this number over all births in that year, as well as future births, yields a total increase of 1.2 million life-years for each yearly drug approval. Lichtenberg estimates that for each extra dollar spent on prescription drugs, $4.5 is gained through productivity enhancement, while each extra dollar spent on drugs reduces other health related expenses by almost $4.

It is also important to note that there is a substantial rate of depreciation in the value of old drugs, implying that future innovation is essential for the gains in health and wealth to be sustainable. Consistent with the findings of Lichtenberg, Murphy and Topel (2003) cite estimates that impute $5.1 trillion in economic value to new discoveries yielding a 10% reduction in the death rate for heart disease, and $4.4 trillion economic value to new discoveries yielding a 10% reduction in the death rate for cancer.

3 Weak IPRs and the origin of generic competition

3.1 Patents and data exclusivity

IPRs in the pharmaceutical industry mainly rest on two instruments, patents and data exclusivity. Patents are usually given for 20 years from the day the patent is accepted by the national patent office. For most innovations, holding a patent is equivalent to having marketing authorization and market exclusivity for a certain period of time. For NCEs, however, holding a patent can be quite disconnected from having marketing authorization. In fact, it can take 10 years, on average, before a newly patented medicine reaches the patient's bedside. After receiving a patent, the innovator must prove the safety and efficiency of the new drug to the regulatory authority.

In order to prove safety and efficiency of a new drug, pre-clinical and clinical tests must be performed. The results of these tests, conducted on animals and humans, are reported in the registration dossier prepared for the regulatory authority. Because of the large investment in time and money needed to successfully gain marketing approval through clinical trials, the data generated during these testing phases is kept confidential and cannot be exploited by potential competitors for a certain number of years. This protection is referred to either as data exclusivity or data protection.

Data protection is an IPR that is distinct from a patent right. New drugs that are not patented or have an expired patent can be protected by data exclusivity. When data protection expires, a competitor can rely on the safety and efficiency tests performed by the innovator, and in the possession of the regulatory authority. If the competitor can show bio-equivalence to the pioneer drug, no further tests are required. The competitor, most often generic firms, can then enter the market, saving millions of dollars in pre-clinical and clinical trials. The significantly lower level of investment needed for a generic to gain marketing approval directly translates into a lower price in that class of medicine.

Because of the high costs in time and money of gaining marketing approval from the regulatory authority, and the contentious legal environment surrounding patents, data exclusivity is fast becoming the dominant IP tool in the pharmaceutical industry. Increasingly stringent requirements for clinical trials have reduced the patent life of innovative drugs. The average patent life remaining after marketing approval in 2001 was 7.8 years, instead of the original 20 years of patent protection (FDA 2002). In comparison, other industrial sectors enjoy an average patent life of more than 18.5 years.

The last 10 years have also witnessed an increase in legal patent disputes between generic and research-based pharmaceutical companies. Generics have been quite successful in challenging patents in the U.S. and in Europe and have a strong incentive to do so. In the U.S., the first generic to challenge a patent is given 180 days of market exclusivity. According to the U.S. Federal Trade Commission (FTC), generics have a 75% success rate in challenging patents.

For most drugs, patent protection goes beyond data protection. However, if the testing period has been extremely long, or if the drug does not have full patent protection, data exclusivity can be the only form of IP. For example, Eprex from Jancen Cilag and Arava manufactured by Aventis had data protection beyond patent life by 1 and 2 years, respectively. Taxol manufactured by Bristol-Myers Squibb (BMS) is protected only by data exclusivity. BMS does not hold a patent since Taxol was licensed to BMS from the U.S. National Cancer Institute.

3.2 IPRs in the US

Perhaps the most important relatively recent U.S. legislation that altered the role of patent protection and data exclusivity in the pharmaceutical industry is the Hatch-Waxman Act. The Hatch-Waxman Act of 1984 granted generic companies easier access to the drug market. The ''Bolar'' clause derived from the Hatch-Waxman Act gave generics the right to start testing bio-equivalency even before patent expiration, so that generics can enter the market almost immediately upon patent expiration.

The Hatch-Waxman Act did, however, also recognize the need to further protect market exclusivity for research-based pharmaceutical companies. The law restores part of the patent life lost by innovators in the process of obtaining marketing approval. The maximum patent life allowed under the law is 14 years regardless of the time spent on testing. A maximum of 5 years of patent life can be restored. Grabowski and Vernon (1996) find that the average patent extension is 2.33 years for NCEs introduced in the first half of the 1990's.

A FTC study on the impact of the Hatch-Waxman Act on competition between generics and innovators found that since passage of the Act, generic market share has grown from 19% in 1984 to 55% in 2004. It took an average of 19 months for generics to gain marketing approval between 1984 and 1994, and the probability of success in getting

approval was very high. For brand names whose patents expired between 1994 and 1997, generics captured 64% of the market share within a year, and 73% after 2 years. Prozac became a typical example of fierce generic competition. One month after generic introduction, the brand name lost 80% of its market share.

Note that another significant advantage that generics have in the drug market, beyond the ability to ''free-ride'' on test data generated by innovators, is that they observe the profitability of innovative pharmaceuticals and imitate only the successful ones. This fact can be especially troublesome for the profitability of R&D. As mentioned earlier, the profits generated by blockbusters cross-subsidize many other R&D investments.

3.3 IPRs in Europe

It is interesting, but perhaps not surprising, that the relationship between IPRs, the incentive to innovate, and competition in the pharmaceutical industry is more complex in Europe than it is in the U.S. Most European countries have a national public health care system, and price controls and parallel importing are routinely used as public policy tools, especially when it comes to blockbuster drugs. Consequently, European pharmaceutical companies have substantially decreased their R&D expenditures over the past decade and have turned to the American market for the introduction of new drugs (see Kingham and Castle 2000).

In Europe, an innovator can gain marketing approval either at the European level, through the so-called Centralized Procedure, or through national regulatory agencies via the Decentralized Procedure. Approvals at the European level allow the innovator to market the product in all member states. This centralized procedure is mandatory for all biotech products and optional for other innovative products. At the European level, 10 years of data exclusivity is granted. This is double the number of years of data protection offered in the U.S.

In the Decentralized Procedure, products can also gain marketing approval throughout the European Union via the Mutual Recognition Procedure (MRP). In the MRP, a marketing application is filed in a particular member state, called the Reference Member State (RMS). After gaining approval in the RMS, the innovator applies through the MRP for marketing authorization in all other member states. The approval to market the drug in other member states is not automatic and a Concerned Member State (CMS) can refuse marketing approval. In 2000, 36% of the drugs applying through the MRP did not obtain approval in at least one CMS.[4]

In the Decentralized Procedure, the innovator is granted data exclusivity that varies between 6 and 10 years, depending on the policy of each member state.[5] The period of data protection is essentially measured from the first marketing authorization within the EU. When data protection expires in the RMS, generic firms are allowed to file for marketing approval in that state, and through the MRP, they may gain marketing approval in other member states in which data protection has not yet expired. Further, when data protection has expired in a particular member state, applications by generics will be accepted, even if the patent has not expired. The patent holder is responsible for bringing an action for

[4] See IMS: http://www.ims-global.com//insight/news_story/0111/news_story_011106.htm.

[5] Belgium, France, Germany, Italy, The Netherlands, Sweden and the United Kingdom have a 10-year limit. Austria, Denmark, Finland, Ireland and Luxemburg have a 6-year limit. Greece, Spain and Portugal have a 6-year limit or until expiration of the patent, whichever comes first.

infringement against the generic firm. These IPR rules in the Decentralized Procedure have increased the incentive of pharmaceutical companies to file marketing applications in the biggest economies first.

With the enlargement of the EU in 2003, harmonization of data protection standards among EU member states caught the attention of policymakers. The EU Council decided that the 10-year data exclusivity clause in the Centralized Procedure could be further delayed by 1 year if the innovator could show that the medicine is an innovative treatment. For drugs registered in the Decentralized Procedure, data exclusivity should be 8 years for all member states but could be lengthened with an extra 2 years of market exclusivity. This rule is often referred to as the 8 + 2 formula. Within the two extra years, generics would be able to start the registration process, and launch their product as soon as the patent expires. The 8 + 2 formula was apparently motivated by the ''Bolar'' provision of the U.S. Hatch-Waxman Act. The European Council is hoping that these reforms will revive R&D activities of the pharmaceutical industry in Europe.

3.4 IPRs worldwide

Data exclusivity and generic competition that derives from its violation has also become a central issue in international forums. In April 1994, the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement was signed by member states of the World Trade Organization (WTO). Article 39.3 of the TRIPS agreement states that, ''*Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.*''

The length of data exclusivity is not clearly established in the TRIPS agreement, and this lack of definition has caused some signatories to almost totally ignore the data protection clause. For example, TEVA, the premier Israeli generic firm continues to have liberal access to data produced by research-based pharmaceutical companies in Israel. This lack of data protection has caused a substantial reduction in R&D expenditures by research-based pharmaceutical companies in Israel, and has allowed TEVA to grow into one of the largest generic multinational pharmaceutical companies in the world.

Current government and supra-government intervention in the pharmaceutical industry that legislates rules and exceptions to IPRs, such as data exclusivity, has given rise to a complicated competitive and legal environment that continues to harm innovation. Thus, policymakers might want to redirect their focus onto the determinants of development costs and its relationship with the institutional structure of drug approval. Directly promoting lower development costs would appear to be a much simpler and more effective route to achieving lower prices and continued innovation in pharmaceuticals.

4 The current drug approval process and its costs

The U.S. market for medicine functioned without any regulatory authority until 1938. The idea of a public regulatory authority in the US arose after the appearance of a toxic drug on the US market, elixir Sulfanilamide, which killed 107 people. A fear of unsafe drugs on the

Table 1 Duration and success rate for new chemical drugs[7]

	Pre-clinical	Phase I	Phase II	Phase III & FDA Approval	Total
Probability of success	.1%	80.7%	57.7%	56.7%	.03%
Successful duration (in months)	42	19.7	29.9	47	96.6

European market, fueled by the ''thalidomide'' affair in the 1960's that led to fetal deformation when used by some pregnant women, motivated the European Commission to adopt standardized regulatory assessments to assure equivalent national regulatory procedures across member states.

The publicity surrounding the discovery of an unsafe drug in the market leads to a public outcry that engenders high political costs. The missed gains from new medicines that are delayed or refused are, on the other hand, more difficult for the public to discover. Thus, government employees in national regulatory agencies have an incentive to err on the side of caution. This asymmetry may lead regulators to allocate too many resources to the prevention of unsafe drugs, raising approval costs beyond socially optimal levels, and delaying or completely preventing the marketing of many safe drugs.

Regulatory authorities allow new medicines or vaccines to be sold to the public only after extensive pre-clinical and clinical trials are performed. These trials examine the safety, quality and efficiency of the new drug in curing diseases. The FDA (2002) estimates that it takes, on average, 8.5 years to bring a drug to the patient's bedside.[6] Other estimates are substantially higher. DiMasi (2001) and Adams and Brantner (2003) estimate the duration of new drug development, from the beginning of the human testing phase to approval, to be 10.2 and 8.05 years, respectively. Dranover and Meltzer (1994) find that it takes 13.5 years to develop a new medicine.

In general, the current drug development process is composed of four distinct stages. The first stage, pre-clinical tests, is usually conducted before the innovator files an Investigatory New Drug (IND) with the regulatory authority. Pre-clinical tests include genetic analysis and animal testing, and last 3.5 years, on average. Many drugs fail during the first stage. According to the FDA (2002), only one out of 1,000 drugs pass the pre-clinical stage.

For the few drugs that pass the pre-clinical testing stage, and review by the regulatory authority, the drug enters human clinical trials, composed of three different phases (I, II, and III). Phase I is carried out on a group of 20–80 healthy volunteers to primarily test the safety of the product. Phase II includes several hundred patients afflicted with the disease. Phase III is an extension of Phase II on a larger number of patients, usually between several hundred and a thousand.

Table 1 reports the average number of months spent in each stage, and the probability of success.

As Table 1 shows, the probability of successfully moving from one phase to the next, conditional on reaching that phase, is not monotonic. In the later phases of development, the probability of success decreases. The length of time spent on development and the

[6] See: http://www.fda.gov/fdac/graphics/newdrugspecial/drugchart.pdf, last accessed December 2004.
[7] See Abrantes-Metz et al. (2003).

probability of success is also not a function of the size of the firm. The ''big-pharmas,'' as measured by the number of drugs that the firm has in development, do not have a clear advantage over ''non-big pharmas.''[8]

After successful completion of clinical tests, the national regulatory authority must approve the new drug. This latter process lasts, on average, one year and a half.

After gaining this last approval the new medicine can be introduced to the market, although further post-approval tests must be conducted to detect adverse outcomes and long-term effects. In Europe, approved new drugs are further delayed because of the existence of government controlled health care systems. Each government has to determine the reimbursement level for each new drug, causing additional delays of several months to several years.

The length of time it takes for new drugs to enter the market, and the consequent cost to society of delays, eventually became a recognized issue by national regulatory agencies. Concern for delays led to the passage of special legislation intended to accelerate the process. In the 1990s, the FDA adopted two new programs: ''fast-track approval'' which expedites review of marketing approval for drugs treating serious and life-threatening diseases, and ''accelerated approval'' for products that provide significant improvement over existing therapies.

Europe has also implemented similar programs. The European Agency for the Evaluation of Medicinal Products (EAEMP) implemented a target time of 210 days for marketing approval of ''orphan drugs'' intended for the cure of rare diseases. In 2003, the goal was reached with an average approval time of 190 days (EAEMP 2003). In addition, ''orphan drugs'' were allowed to have smaller and shorter clinical trials. In 1999, orphan drugs were approved after testing on an average sample of 588 patients. Non-orphan drugs are tested on over 5,000 patients.

Although the measures adopted by regulatory authorities in the US and Europe, for a few selected products, are commendable, much further progress in shortening development times of new medicines is possible. Note that R&D requires the payment of salaries, the purchase of animals and expenses on equipment. The firm must invest its own capital or borrow capital from external sources in order to finance its R&D activities. In either case, the length of time before commercialization directly impacts the financing cost component of R&D activities through opportunity costs or payment of interest. Shorter development times would directly translate into lower costs and lower prices.

Estimates of the direct monetary costs of developing a new drug show that development costs are not decreasing over time, despite the recent efforts of regulatory agencies, but are rather dramatically increasing. An early study by Hansen (1979), using a sample of NCEs entering human testing between the years 1963 and 1975, found that the total cost of bringing a new drug to the market is $119 million. DiMasi et al. (1991) using a similar sample between 1970 and 1982, found the total development cost to be $231 million, representing a 94% increase in R&D costs between the two cohorts. The Office of Technology Assessment (1993) confirmed the figures reached in these studies. The OTA explains the rapid rise in R&D costs in the 1970s and 1980s by increases in labor costs, the size of clinical trials and the costs of animals used in pre-clinical testing.

[8] Because of their novelty, fewer studies on duration and probability of success have been conducted for biological drugs. Biological drugs first appeared in the market in 1984, and by 1994, only 29 biological entities were marketed in the U.S.

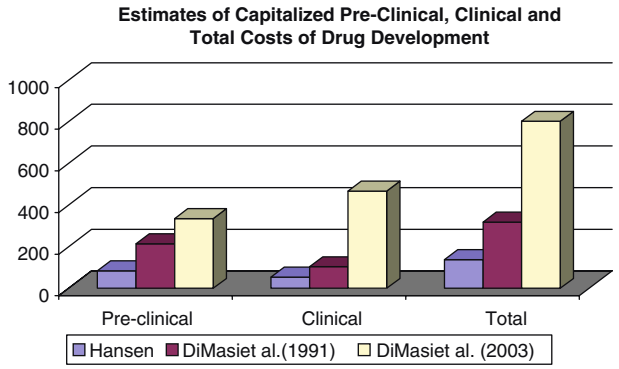

Fig. 1 The costs of drug development

A more recent study by DiMasi et al. (2003) uses a random sample of 68 drugs, from 10 different pharmaceutical firms, that entered clinical testing between the years 1983 and 1994. DiMasi et al. use the same methodology as earlier studies and find that the cost to the firm of having a drug approved is $802 million dollars (in 2000 dollars). Including the post-approval cost of testing increases the figure to $897 million.

DiMasi et al. also broke down the costs by development phase for their previous and current studies, and estimated the allocation of R&D resources by testing phase for the Hansen study. The results are summarized in Fig. 1.

The dramatic rise in the cost of developing a new drug is mainly explained by the increase in size and complexity of clinical trials and higher labor costs. According to data compiled in the US between the years 1981 and 2001, the increase in trial size was 7.47% annually (see OTA 1993; Peck 1997; CMR 2000). As reported by DiMasi (2003), clinical trial complexity rose by 4.8% annually from 1992 to 2000. Labor costs rose because total R&D employment increased, as did the average salaries for scientists and researchers. The Bureau of Labor Statistics projects this trend to continue over the next decade.[9]

The exceedingly high and increasing costs of drug development, combined with artificially low market prices through price controls and generic competition, places privately initiated drug innovation at risk. It is, therefore, critical that policymakers consider alternative institutional arrangements for drug approval that can effectively bring down costs, as well as prices, and that preserve the incentive to innovate.

5 Privatizing the drug approval process

5.1 Federal drug administrations and monopoly power

Drug approval in the U.S. can only be gained through the FDA, a pure public monopoly. The European situation is quite different. The existence of the MRP allows for a measure of competition between national regulatory authorities. A pharmaceutical company can choose the country in which to file for drug approval. Licensing fees are paid only to the first state that approves the new drug, creating an incentive for regulatory agencies in

[9] See BLS ''Pharmaceutical and Medicine Manufacturing,'' NAICS 3245.

different European countries to compete. The UK, for example, streamlined its regulatory requirements under the Thatcher government and attracted pharmaceutical companies to seek approval there.[10] This competitive environment gave rise to a convergence in approval times between countries. Approval times decreased in the UK and Germany by almost 70% (see Thomas et al. 1998). The European experience clearly demonstrates that competition among approval agencies can succeed in reducing approval times and overall development costs.

However, the current European MRP faces many problems. For example, marketing approval is rarely given in all European countries. From 1998 to 2001, the number of Member States included in the MRP was, on average, less than half (Feick 2002). Concerned States that do not receive fee payments have little incentive to accelerate approval. It may even be in the interest of Concerned States to delay approval, in the hope of signaling to the market that the Reference State was faster to approve, but fell short of insuring mutual recognition. In fact, the Decentralized Procedure took 6 months longer, on average, than the centralized procedure in 1999. The main component of delay in the MRP is disputes between national regulatory agencies. The European CPMP that reviews disputes continues to experience an increase in time to final decision.

The fact that mutual recognition has to be discussed and approved at many bureaucratic levels slows the overall drug approval process and does not foster a truly competitive environment. Moreover, national regulatory agencies still have an approval monopoly within a State. This allows national agencies to strategize against each other, delay approval times, and hold the citizens of the country ''hostage''. A truly competitive market in drug approval among monopoly national regulatory agencies may be difficult to establish. Further devolution of drug approval to several (or many) competitive certification bodies within each state seems necessary.

Note that the idea of competitive certification bodies is not entirely new. For example, The Progress and Freedom Foundation (PFF) developed a proposal in 1996 in which the idea of ''Drug Certification Bodies'' (DCBs) was advanced. DCBs were envisioned to work independently of central regulatory agencies and a national board, similar to the Joint Commission on Accreditation of Healthcare Organizations, would certify DCBs. In the PFF plan, the responsibility of final drug approval remains with the central regulatory agency. DCBs only compete in offering drug approval services to their clients (pharmaceutical companies) based on the speed of their own approvals and their quality as measured by the fraction that gain final approval from the central regulatory agency.

The PFF plan is interesting but it falls short of full competitive potential. The incentives of the central regulatory agency would still lead to an overly cautious approach to final drug approval. Anticipating this problem, the FPP plan proposes the establishment of an independent commission that would oversee disputes between DCBs and the central regulatory authority. In other words, the FPP proposes a variation on the European CPMP for disputes within countries. This latter aspect of the FPP plan is its weakest link.

A better system, in our opinion, would be one in which DCBs are responsible not only for assessment of safety and efficiency, but also for final drug approval. There is little need for a central agency with final approval powers. The safety and efficiency of drugs could be reliably determined as a result of market mechanisms and legal recourse. The importance of reputation in maintaining clients and attracting new ones, the existence of a free press

[10] As a consequence, the Medicines Control Agency (MCA) was able to raise half of its income from fees charged to the pharmaceutical industry.

engaging in investigative journalism, and expected penalties via the legal system for corrupt and dangerous decisions by DCBs, should be sufficient to establish a well-functioning market.

5.2 Is privatization of drug approval Kosher?

It is interesting to note that a competitive free market in product approval and certification, analogous to the competitive market in drug certification that we propose here, has thrived for centuries among observant Jews that adhere to the laws of Kashrut (kosher food). According to Jewish Law, certain categories of food are forbidden for consumption, meat and dairy products may not be mixed together within a single food product, animals must be slaughtered in a specific way, and the meat must be properly soaked and salted before being cooked. Religious Jews are required to eat food that adhere to these standards and that has been verified by religious authorities for compliance.

Violation of Jewish dietary restrictions may not lead to physical death, as may be the case in dangerous medicines, but many adherents fervently believe that non-compliance could permanently damage the soul. In order to aid religious Jews in their compliance, Kashrut certification boards (KCBs) have arisen that certify food products for compliance with religious standards. KCBs compete against one another and each board has its own easily identifiable label. KCBs attract a following based on reputation and trust. Moreover, religious Jews can easily identify KCBs that adhere most closely to their own personal preferences for stringency. There is a natural distribution of personal preferences for stringency to dietary restrictions within the population of religious Jews, and this distribution is reflected in the distribution of types of KCBs that operate in the market.

The sustainability and success of KCBs for hundreds of years, spanning nations, is a good illustration of how DCBs could thrive in the absence of an over-riding central regulatory agency. Some individuals may want an extremely safe medicine that was given approval by a known conservative DCB, just as religious Jews may want to eat food products that are certified by the most stringent KCBs and that are consequently the most expensive. Other individuals may be less risk averse, less willing to pay for, and in more dire need of particular medicines. These latter individuals would have the option of using a cheaper, ''riskier'' medicine approved by a less stringent DCB.[11]

If individuals were allowed to determine for themselves the optimal amount of safety (or stringency) required, according to their own preferences and budget constraints, the distribution of types of DCBs arising in a competitive drug approval market would likely reflect this heterogeneity, and lead to increases in consumer welfare. Note that religious Jews often consult with their spiritual leaders in order to choose the KCB that most closely reflects their preferences for stringency. Local physicians could serve an analogous role helping individuals to navigate between the different drug certifications on the market.

It is also reasonable to assume that a market in information on DCBs would quickly arise, easing access to information and fostering transparency. KCBs have had to be very careful in maintaining their reputations, and fraud has rarely been a problem. A KCB

[11] Note that AIDS groups are now lobbying for a relaxation of drug approval requirements. See for example the Gay Men's Health Crisis (GMHC) at http://www.aegis.com/pubs/gmhc/1996/GM100503.html.

that misleads its consumers goes out of business quickly.[12] Today there are more than 100 KCBs as well as magazines that report changes in KCB standards and possible corruption.

It is, therefore, easy to imagine that DCBs, in a vigorously competitive market, would find it optimal to build a history of good drug approvals and to develop a trustworthy relationship with their consumers. A DCB that bends to pressure from pharmaceutical companies, and which is comprised of members who are ''captured'' by pharmaceutical companies, would likely be quickly exposed. The marketability of the pharmaceutical companies future products would consequently suffer.

The existence of competing DCBs in a well-functioning market with no central approval agency should have a large depressing effect on the costs of R&D required for the introduction of a new drug. Unnecessarily stringent rules and procedures for clinical tests, dictated by overly cautious central agencies, would be eliminated along with bureaucratic inefficiencies. In other words, a well-functioning market in drug approval will bring down the costs of R&D and drug prices, just as privatization has led to cost decreases, lower prices and accelerated innovation in other sectors of the economy.

Note also that a significant decrease in R&D costs through privatization could have a large impact on the extensive margin. Currently, small biotech firms are finding it difficult to raise sufficient funds to survive the lengthy and costly drug development process. Fostering the entry of biotech firms into the pharmaceutical industry is important for more innovation as well as more competition with traditional pharmaceutical firms. In the U.S, 30% of all drug approvals in 2002 went to biotech drugs.[13] In 1999, they only represented 6%. According to the European Commission, half of the new medicine in development today is based on biotechnology.

5.3 Potential pitfalls to privatization and unlimited data exclusivity

A competitive drug approval market that embedded unlimited data exclusivity would obviously engender fierce opposition from generic firms. It might also face opposition from consumer groups in favor of compromising data protection on non-economic grounds. One argument rests on the consumers right to know test results. Ollila and Hemminki (1996) make a case for more transparency in this regard. Admittedly, the existence of competing DCBs would not totally resolve this problem but consumers would at least have the right to choose which DCB to trust, and arguably have more indirect knowledge of the reliability of a DCB's tests than under the current centralized regulatory system. The profitability of the DCB would serve as a strong signal of the reliability of their approvals.

Another non-economic argument against granting unlimited data exclusivity is that it may lead to ''needless'' replication of testing on humans and animals (see Dukes 1996). In order for a potential entrant to gain certification of a competing drug, clinical trials would have to be repeated even though similar trials were already performed and shown to be successful. This could expose patients to potential hazards. However, it could also be argued that these ''additional'' tests are not at all unnecessary. They could help further

[12] Many big food companies demand certification from KCBs with the highest standards in order to appeal to the largest number of potential consumers.

[13] This figure includes monoclonal antibody and recombinant protein products. (SMD, rDNA and mAb therapeutics).

establish, or even call into question, the safety of an already certified class of medicine.[14] In any case, the much lower costs of conducting trials, resulting from the privatization, will ease the burden of repetition.

Note that arguments for lengthening the period of data exclusivity have been advanced before in the economics literature. For example, Grabowski (2004) holds that in order to reduce uncertainty, lower litigation costs, and improve R&D incentives in the US, the US data exclusivity period should be at least doubled to coincide more closely with the European regime. This line of thought sees the optimal length of data exclusivity being determined by a balance between the marginal cost of decreased innovation incentives (which diminishes over time) and the marginal benefit of lower drug prices achieved through generic competition.[15] In our proposed system, lower drug prices come about through privatization, a completely different mechanism. Thus, there is little extra benefit in limiting data exclusivity as long as the cost of performing clinical trials is ''reasonable''.

6 Conclusion

Obtaining drugs at lower prices is a priority public policy issue. However, ensuring continued pharmaceutical innovation is also critical for increases in longevity, better health, higher productivity and economic growth. Balancing the price of medicine against incentives for continued drug innovation is a difficult challenge facing legislators.

This paper argues that a reduction in the price of pharmaceuticals could be brought about by fostering competition in the drug approval process. Weak data protection laws and generic competition is not necessarily the best solution to the drug-price problem. Artificially low prices combined with exceedingly high and ever-increasing drug development costs could lead to substantially lower levels of pharmaceutical R&D, innovation and new life-saving medicines.

We maintain that a better solution to the drug-price problem lies in reforming the monopolistic regulatory drug approval process. The abolishment of national drug administrations and their replacement with private competing drug certification boards, with the power of final marketing authorization, could decrease the overall costs of drug development without compromising public health, and without discouraging innovation.

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[14] Recent technological advancements may render animal testing obsolete in the near future. In the UK alone, $477 million per year is spent on developing new technologies that could replace the need to perform animal-trials.

[15] Reiffen and Ward (2002) estimate that considerable price reductions occur after 8 to 10 generic firms have entered the market.

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