Article

Just Rules for Innovative Pharmaceuticals

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Abstract: Globalized in 1995 through the TRIPs Agreement, humanity’s dominant mechanism for encouraging innovations involves 20-year product patents, whose monopoly features enable innovators to reap large markups or licensing fees from early users. Exclusive reliance on this reward mechanism in the pharmaceutical sector is morally problematic for two main reasons. First, it imposes a great burden on poor people who cannot afford to buy patented treatments at monopoly prices and whose specific health problems are therefore neglected by pharmacological research. Second, it discourages pharmaceutical firms from fighting diseases at the population level with the aim of slashing their incidence. These problems can be alleviated by establishing a supplementary alternative reward mechanism that would enable pharmaceutical innovators to exchange their monopoly privileges on a patented product for impact rewards based on the actual health gains achieved with this product. As such, an international Health Impact Fund (HIF) would create powerful new incentives to rapidly develop remedies against diseases concentrated among the poor, provide such remedies with ample care at very low prices, and deploy them strategically to contain, suppress, and ideally eradicate the target disease. By promoting innovations and their diffusion together, the HIF would greatly enlarge the benefits, and thereby also the cost-effectiveness, of the pharmaceutical sector, especially in favor of the world’s poor.

Keywords: disease; diffusion; financing; health; Health Impact Fund; impact rewards; incentives; innovation; justice; monopoly rewards; pandemic; patents; pharmaceuticals; poverty; vaccines

1. Introduction: The COVID-19 Pandemic

In a pandemic, speed matters. Delay means more deaths and infections, with increased risk of new virus mutations.

Vaccinating the world as fast as possible is a three-stage relay race: effective vaccines must be developed, tested and approved, manufactured at scale, and then delivered all over the world.

As epitomized by the amazing work of Özlem Türeci and Uğur Şahin, innovators have exceeded expectations in the first stage, bringing several highly effective vaccines to market in under a year. But we have been less well served in the other two legs of the race: manufacturing scale-up and strategic delivery. Over one-third of humanity, mostly the poor, are still not fully vaccinated and thereby breeding grounds for new variants that may endanger us all. Still evolving new variants that pose novel health-care challenges, COVID-19 continues to kill at a monthly rate of 50,000 and to infect at a monthly rate of 20 million [1].

This outcome could be expected if pharmaceutical firms were pure profit maximizers. They would then have the following interests:

- Quickly develop new pharmaceuticals that can effectively protect individuals from harm—without impeding the proliferation of the disease;
- Scale up production of such new pharmaceuticals cautiously: while safeguarding proprietary technologies and know-how, avoiding wasteful excess capacity, and maintaining a favorable demand-supply imbalance to sustain high prices;
• Prioritize buyers who are offering to pay more and reject potential buyers who are only marginally profitable, might erode the product price, and are more useful at spreading and prolonging the epidemic with the potential emergence of new disease variants;
• Forestall regulatory interference in—and public awareness of—their profit-maximizing stratagems by making it appear that suppressing the disease as effectively as possible is really their most profitable strategy or, more credibly, that they are wholeheartedly dedicated to its eradication, regardless of profits.

Actual pharmaceutical firms are not focused on profit alone. However, they are surely not indifferent to profit either. Profit is what Wall Street—hedge funds and other large professional investors—care greatly about; and such shareholders have the power to reward, to discipline, and even to fire non-compliant CEOs and are forever breathing down their necks. It is thus unsurprising that, on closer inspection, our experience with the COVID-19 pandemic is uncomfortably close to what would have happened in a world of exclusively profit-maximizing firms.

To succeed better against pandemics, do we need a moralization of pharmaceutical companies? Should we place this industry under public control and ownership? Must we perhaps even abolish capitalism?

There is a more practical solution that ought to be explored with priority: modify the rules of the pharmaceutical sector so that profits are better aligned with social benefit. The present rules reward pharmaceutical firms through substantial price markups which they can earn under protection of their 20-year monopoly patents. Under this regime, firms profit when a pandemic is spreading more widely, profit when it lasts longer, profit when it evolves new variants, and profit when remedies remain in short supply. We should modify the rules so that firms earn the most when they achieve the best outcome for the world: rapid containment and suppression of the disease.

What kind of reward system might provide optimal incentives to pharmaceutical firms? The most important objective here is to motivate firms to fully include poor people in a global population-level strategy. For this inclusion to work, an effective new treatment must be cheap enough to be affordable to all and delivering it even to the poorest must be profitable enough for firms to want to do so effectively and comprehensively. In our world of widespread severe poverty, these two requirements are not co-satisfiable. There is no sales price that is low enough to fulfill the first requirement and high enough to fulfill the second. This problem can be resolved by setting a very low or zero sales price complemented by a delivery premium tied to the health impact achieved with a pharmaceutical’s diffusion.

Assigning equal value to all human lives, this premium should be wholly independent of the economic position of the person or country served and instead be based solely on how the given treatment affects the health prospects of the recipient and of other persons who might (directly or indirectly) become infected through this person. In the case of vaccines, the aggregate health gain from treating a given group of persons depends on facts about the vaccine administered, the time of vaccination, the persons vaccinated, and their environment (including existing disease vectors).

It would not be feasible to assess the specific health gain achieved by each vaccination event individually. Fortunately, this is not necessary because the objective is not to ascertain the whole causal truth but to provide optimal incentives to firms. For this purpose, reasonable approximations suffice. The reward should be sensitive to the extent to which a vaccination reduces the probability that its recipients will become infected and will infect others, and sensitive also to the extent to which it reduces the harm its recipients will suffer if they become infected despite having been vaccinated. These sensitivities result in a larger payment for vaccinations that are delivered sooner or provide better protection, including protection that works against more variants, remains effective for longer, or makes the vaccinated person less infectious to others.

These sensitivities also entail higher rewards for delivering vaccinations to persons who are at higher risk of being infected or of infecting others—persons in high-incidence
countries or regions, for instance, and persons in more interactive professional groups. However, such incentivizing differentiations in the reward per vaccination should be made only insofar as the vaccine provider is in control of the relevant delivery decisions. If the vaccine supply is allocated and delivered by a national health service or by some international organization (such as the WHO or COVAX), then the reward should more simply be based on time of delivery and, mainly, on vaccine quality as manifested in its average impact given the general risk level prevailing in the relevant (national, regional, or global) delivery population.

Faced with the COVID-19 epidemic, a timely guarantee that the vaccination of every vaccine-eligible person will be generously rewarded would have required a large reward pool, around EUR 50–100 billion, 0.1–0.2% of the combined gross national incomes of the high-income countries. This is substantially more than the few billion dollars that COVAX has had at its disposal, enabling it to deliver 1.56 billion doses thus far [2]. However, the amount needed to back a guarantee of universal vaccination is also vastly smaller than the economic damage this pandemic has been causing worldwide and the national economic stimulus packages it has triggered, which are valued at several trillion euros.

The proposed universal vaccination guarantee would instantly remove any anxiety about whether vaccinating humanity’s poorer half will be profitable. It would incline competing pharmaceutical innovators to seek to develop a highly effective vaccine and then to ramp up the manufacture process quickly to capture the largest feasible share of the reward pool. When a firm’s profit margin is essentially fixed, based on its manufacturing costs and the effectiveness of its vaccine, then the firm’s profit depends on speed and quantity, and on how many vaccinations are performed with its product. Each firm has an incentive then to deliver large quantities of its product as soon as possible. Firms would compete to use all available manufacturing capacity around the world while also expanding such capacity toward accelerating deliveries.

These desirable incentives would be disturbed if some buyers were disposed to offer substantially higher per-dose payments to jump the queue. Such offers would cause departures from the optimal vaccination sequence—affluent people at minimal risk of infection would be vaccinated before even frontline health workers in low-income countries. The prospect of such offers could also undermine the incentive for firms to deliver with maximum speed: slowness of manufacturing and delivery prolongs the demand–supply imbalance that encourages and sustains a bidding war among rich buyers. Any such disturbance would make it harder to contain and suppress the pandemic globally, and richer countries ought therefore to subordinate their national self-interest to the best global strategy by agreeing to draw their vaccines solely from the single vaccine flow created by the global reward pool. In the present pandemic, they have failed to do so. Thus far, only about 9% of vaccine doses have been delivered through COVAX—most of the rest through a secretive bidding war among mostly affluent buyers [2]. No wonder then that the relevant pharmaceutical innovators are in no hurry to ramp up manufacture to immunize the world: potential profits from vaccinating the poorer half are small and doubtful, while large profits beckon from a prolonged demand–supply imbalance.

A permanent pay-for-performance scheme would encourage firms to build capacity for the next pandemic. Numerous emerging infections have threatened humanity over the last few years—SARS, Zika, and Ebola have menaced our globalized world and then receded. Like the present pandemic, they underscore the need for new incentives that are better aligned with the needs of humankind, incentives that would effectively stimulate a rapid vaccine roll-out, with powerful rewards for fast product development, manufacturing scale-up, and delivery. While monopoly rewards tempt innovators in various ways to put profits above people, performance rewards could align profits with human needs, thereby making the business of innovation much more equitable in terms of research priorities and access to its fruits, while inducing innovators to do well by doing good. Such new incentives should also target the still enormously harmful diseases of poverty—tuberculosis, malaria,
diarrhea, pneumonia, etc.—which routinely kill millions and pose explosive risks due to evolving mutations and drug resistance.

2. Excessive Reliance on Monopoly Rents

The COVID-19 pandemic has drawn much attention to the rules governing pharmaceutical innovation. The most important rules were globalized in 1995 through the TRIPS Agreement, Annex 1C of the founding treaty of the World Trade Organization. A key provision of TRIPS (Articles 27, 28, and 33) entitles innovators to 20-year product patents that enable them to prevent others from making or selling their product in the relevant jurisdiction. Thus protected from competition, innovators can sell their patented product at high markups or charge high royalties for rights to manufacture or sell it. Such earnings allow them to recover, with profit, their up-front investments into research and development (R&D), patenting, and pursuing regulatory approvals. These fixed costs of innovation are thus, in effect, paid for by early buyers of innovative products, who buy them while they are still under patent.

The monopolies awarded under the patent regime provide strong innovation incentives. However, they also have important drawbacks. Because pharmaceutical firms earn their rewards from user-focused decisions, their innovative activities are focused on generating benefits for users while largely ignoring both positive and negative externalities. Such firms are simply not rewarded for third-party benefits such as reductions in the incidence of the target disease. On the contrary, they are penalized for any such success insofar as it also reduces future demand for their product. Monopoly rewards are poorly suited to the task of suppressing and eradicating infectious diseases.

Another important drawback is that monopoly rewards lead to exorbitant prices and related neglect of diseases concentrated among the poor. A typical example of exorbitant prices is an important cure for hepatitis C, sofosbuvir, which was introduced in 2013 under the brand name Sovaldi by patentee Gilead Sciences at a price of USD 84,000 per course of treatment, 3000 times the estimated cost-based generic price of USD 28 [3]. In poorer countries, where the upper classes are less affluent and less well-insured, the profit-maximizing price typically is substantially lower—but still unaffordable with the also much lower ordinary incomes there. The reason for this widespread unaffordability is that, even intra-nationally, economic inequalities tend to be large, and demand curves are therefore highly convex [4] (pp. 187–188). The patent holder could lower the price. However, its gain from making more sales would be smaller than its loss from reducing its profit margin. In a world of enormous economic inequalities, both globally and within most countries, pharmaceutical firms do best by selling their patented products mainly to the rich and well-insured. Each year, millions of people suffer and die from lack of access to medicines that generic manufacturers would be glad to mass-produce and sell quite cheaply. Even five years after sofosbuvir’s market introduction, only about 7% of the 71 million persons living with hepatitis C had been treated, while the remaining 66 million remained ill and potentially infectious to others, [5] which, though advantageous to the patentee, poses a danger to humanity and especially to the poor.

Reliant on exorbitant markups, pharmaceutical firms naturally pass up potential innovations that address the specific needs and circumstances of poor people who are unable to afford such high prices. This is documented in the strong correlation between disease-specific R&D investments and the average income of the corresponding patient population [6]. As a result, the world is woefully underequipped with pharmaceuticals against diseases of poverty and with heat stable and pediatric formulations. While male pattern baldness and erectile dysfunction garner abundant research attention and innovator profits, the opposite is true of the 20 notoriously neglected tropical diseases, which afflict over a billion people, [7] and of other major diseases concentrated among the poor, such as tuberculosis, malaria, hepatitis, pneumonia, and diarrhea, which together kill some 6 million people annually [8,9]. Pharmaceutical innovators could massively reduce the global burden of disease by developing and deploying new pharmaceuticals against these
diseases of poverty. Such efforts would produce large positive externalities by reducing the risk of infection as well as the threat from more virulent potential mutations that could trigger pandemics. However, so long as pharmaceutical innovators depend on monopoly markups for their earnings, the lack of effective remedies against the diseases of poverty is likely to persist.

Poor people are especially vulnerable to disease. The FAO reports that, in 2019, 41.9% of the world’s people could not afford a healthy diet at an average cost of USD 4.04 per person per day at purchasing power parity [10] (p. 27) and that, since that time, real (inflation-adjusted) world food prices have risen by 66% (May 2022) [11]. Large percentages of humankind also lack safe drinking water [12], adequate sanitation [13], adequate shelter [14], electricity [15] and basic education [16,17]. These grave social burdens make the poor much more prone to disease, which in turn reinforces their poverty. Our current international rules governing pharmaceutical innovation reinforce this vicious cycle by excluding the poor from advanced medicines. It is not surprising, then, that the poor end up bearing a hugely disproportional share of the global burden of disease. This is evident in the data from Africa which, according to the World Bank, accounted for over half of the world’s poorest even while it had only 14% of its people [18]. Like other populations, Africans are afflicted by non-communicable diseases such as diabetes, cancer, and cardiovascular conditions; but, unlike others, they bear a much heavier additional burden of communicable diseases such as malaria, HIV/AIDS, tuberculosis, diarrhea, and respiratory infections. Over 90% of the estimated 200–300 million annual malaria cases worldwide are suffered by Africans, [19] (pp. 19, 22) mainly by children under five years of age; and Africa also accounts for two-thirds of all HIV/AIDS cases worldwide. Life expectancy in Africa is more than 11 years below that of the rest of the world [20].

The drawbacks of monopoly rewards can be mitigated by establishing an additional, optional reward mechanism. With contributions from willing countries, this proposed international Health Impact Fund (HIF) would invite innovators to exchange their monopoly rents from any new pharmaceutical for impact rewards as an alternative way for them to recoup their R&D expenses and to make appropriate profits [21]. Innovators would find HIF registration especially attractive for new pharmaceuticals with which they expect to be able to generate large cost-effective health gains but only modest monopoly rents. These would tend to be effective remedies against diseases that are widespread, grave, infectious, and concentrated among poor people. Many of these HIF-registered pharmaceuticals would be ones that otherwise would not have been developed at all.

As a structural innovation in how to stimulate innovation, the HIF would open the way to analogous impact funds in other sectors: agriculture, green technologies, and education, most obviously. It would do so by pioneering a morally compelling idea of social purpose that values the lives of people equally rather than according to their positions on the demand curve (according to what they are willing and able to pay) [22].

3. The Health Impact Fund as an Add-on to the Pharmaceutical Innovation Regime

The global market for pharmaceuticals is currently worth about USD 1.43 trillion annually, 1.7% of the gross world product [23] (p. 5). These annual sales fall under three headings: roughly USD 550 billion are spent on patented pharmaceuticals; USD 250 billion are spent on pharmaceuticals that are off-patent but still sold by their former patentee under the same brand name, benefiting from the name recognition they acquired during their patent period; and the remaining USD 630 billion are spent on generic products [23] (pp. 51–53). Sales prices decline sharply over these three categories, and the vast majority of pharmaceuticals manufactured, sold, and consumed worldwide are generics. Although generics are off-patent, their availability is nonetheless heavily influenced by patent incentives, which condition which innovations are pursued and how they, if and when approved, are introduced into national markets. Many potential pharmaceuticals do not become available as generics because no innovator has found it worthwhile to develop and win regulatory approval for them in the first place.
Adding the HIF to the current regime would make it profitable for innovators to realize the most cost-effective health gains achievable through appropriate investments in pharmaceutical R&D and subsequent product manufacture and delivery. An efficient way of doing this would have the HIF make fixed annual distributions that are divided among registered pharmaceuticals according to the health impact achieved with them in the preceding year. Each registered innovation would participate in ten consecutive annual payouts and then go generic.

Some version of quality-adjusted life years (QALYs), as widely employed and refined in recent decades, could be used as a common metric for comparing and aggregating health impact across diverse diseases, therapies, demographic groups, lifestyles, and cultures. The HIF would create a novel market in which new pharmaceuticals of all kinds would compete in the quest to achieve the most cost-effective health gains (the “lowest-hanging fruits”). Patentees would have their registered products rewarded based on their performance, of which diffusion is an essential part.

By covering R&D costs and innovator profits, the HIF would transform registered pharmaceutical innovations into public goods, whose sales price would be delinked from the fixed R&D expenses and limited to the lowest feasible variable costs of manufacture and delivery. This price cap could be determined through a tender among competing contract manufacturers; or the innovator might issue royalty-free licenses for the manufacture and sale of its product. Because HIF-registration—the shift from monopoly markups to impact rewards—is in each instance chosen by the innovator, it will nearly always enhance innovator profits; and it will always greatly magnify the social benefit achieved with the registered pharmaceutical.

It is crucial for the efficiency of the HIF that it have reliable long-term funding commitments. Innovators considering a high-impact R&D project intended for HIF registration must have assurance that they will get paid during their pharmaceutical’s first ten years on the market. If these rewards are perceived as uncertain, innovators will discount them with the result that the HIF’s reward rate will be higher than necessary.

At least initially, the needed reliable long-term commitments will have to be underwritten by states. States might decide to finance the HIF through an international tax—on airline departures or financial transactions, for instance—or through direct government contributions tied to country population and per capita income. Either way, affluent people should bear the lion’s share of the HIF’s budget, just as they now pay the lion’s share of fixed R&D costs through monopoly rents on patented pharmaceuticals. However, there is one crucial difference: payment through the HIF avoids the need to exclude the poor!

The HIF should include many—ideally all—countries. A larger geographical scope raises the number of beneficiaries of HIF-registered products even while the—normally very large—fixed costs of pharmaceutical R&D remain the same and are spread over a larger number of contributors. Roughly speaking, a doubling of the HIF’s scope can quadruple its benefits by doubling both the number of HIF-registered products as well as the number of human beings with rent-free access to these products.

Over time, a stable, self-adjusting reward rate would emerge on the HIF. When innovators find it unattractive, registrations dry up and the reward rate rises as older innovations exit at the end of their reward period. When the reward rate is seen as generous, registrations proliferate, and the reward rate declines. Such predictable adjustment ensures that the endogenous reward rate equilibrates to a level that is fair between funders and innovators. This reward rate will then also guide decisions about manufacturing and delivery, inducing innovators to make any and all efforts that they expect to be more cost-effective (QALY/EUR) than the going HIF reward rate.

The size of the annual HIF distributions can be set, and possibly revised, to attain the desired level of innovator participation. With annual distributions of EUR6 billion, each registered pharmaceutical would participate in pay-outs of EUR 60 billion over its 10-year reward period. A commercial innovator would register a product only if it expects to make a profit over and above recouping its R&D expenses. There is some controversy over what
these fixed costs per innovation (inflated to account for the risk of failure) amount to. The number of products registered with the HIF would throw light on this question because of the fund’s self-adjusting reward rate. Were the HIF to attract, say, 30 products, with three entering and three exiting in a typical year, this would show that the prospect of EUR 2 billion over ten years is seen as satisfactory—neither windfall nor hardship.

To make creation of the HIF politically realistic, participation must be conceived as optional—not only for innovators but also for funders. If some high-income countries fail to contribute, the HIF should let innovators charge patent-protected high prices on their registered pharmaceuticals in those non-contributing affluent countries. This exception would give high-income countries an incentive to join the funding partnership. This exception would also lower innovators’ opportunity cost of registration and thereby depress the HIF’s endogenous reward rate, making it cheaper for the HIF to attract a given number of registrations. In this way, the missing payments from non-contributing high-income countries can largely be offset by the HIF’s lower cost. With this cost reduction, it becomes realistically feasible for one major country or even a centi-billionaire to initiate the HIF’s founding, even while several high-income countries decline.

Whatever its initial size, the HIF can be expected to expand over time—through accession of new states, economic growth in contributing states, or agreement to raise the contribution rate—and it would then attract an increasing number of new pharmaceuticals. In due course, the HIF might also build an endowment, welcoming contributions from non-state actors (foundations, corporations, individuals, and bequests) and gradually becoming more independent from states.

By contributing to the HIF, states and their citizens would reap offsetting economic benefits of four kinds: savings on (i) registered pharmaceuticals and (ii) other health care costs—savings that also reduce expenses for health insurance, national health systems, and foreign aid—as well as gains in (iii) economic productivity and (iv) associated tax revenues. In addition, the HIF would largely avoid the wasteful expenditures now typical of the pharmaceutical sector: costs for patenting and associated litigation, economic deadweight losses, and costs arising from corrupt marketing practices and counterfeiting. Even more important would be the underlying human benefits: people feeling and functioning better, leading longer and healthier lives, and being less stressed by diseases and premature deaths among their family members, friends, and associates.

4. How the Health Impact Fund Would Guide R&D

The HIF would steer innovators toward developing the products with which the most cost-effective health gains can be achieved—taking account not merely of a product’s direct effects on its users but also of externalities such as the impact of its use on the evolution of its target disease. This would, in the first instance, focus innovator attention on widespread communicable diseases. Even in this area, though, new pharmaceuticals that could be sold in substantial quantities at very high prices might not be registered if they are expected to make more money from conventional monopoly rents. The HIF would thus attract innovators especially to serious communicable diseases concentrated among the poor. The patent system engenders neglect of such diseases because those suffering from them cannot afford the high markups from which pharmaceutical firms derive their earnings. Heretofore understudied, these devastating diseases are ones against which extremely cost-effective gains can be achieved, and the HIF would therefore lead innovators to prioritize them.

In doing so, the HIF would contribute to capacity building in lower-income countries, where these health gains are to be achieved. This includes skills in data collection, conducting clinical trials, and pharmaceutical manufacturing. It also includes skills in pharmaceutical innovation. In researching global diseases such as cancer, diabetes, and heart disease, innovators in the Global North have a large head start, making it difficult for newcomers to compete effectively. Innovators from lower-income countries are much better able to compete, however, in researching potential remedies for diseases of poverty—diseases about which they have extensive local knowledge.
Inducing the development of important new pharmaceuticals against diseases of poverty, the HIF would be a valuable partner for organizations such as the Global Fund, GAVI, Médecins Sans Frontières, Partners in Health, and governmental development assistance operations (such as USAID, BMZ, DFID, and SIDA) by making available to them, at very low prices, new and better pharmaceuticals for their work. The HIF would also engender much deeper and broader knowledge about such diseases and greater capacities for developing additional, more targeted responses, quickly. Innovators would thus be much better prepared to develop and supply pharmaceuticals suitable for confronting emerging threats such as Ebola or COVID-19.

In addition to ending the horrendous neglect of diseases of poverty, the HIF would affect the direction of pharmaceutical R&D in two further ways. The patent system biases innovators to favor developing maintenance drugs over cures, and especially over vaccines which are usually purchased in large quantities by governments, international organizations, or other agencies with substantial bargaining power. By rewarding all health gains equally, regardless of the type of pharmaceutical with which they are achieved, the HIF avoids any such bias. Moreover, by rewarding positive externalities, the HIF would especially encourage the development of vaccines that suppress contagion by not only protecting vaccinated persons but also their contacts.

The patent system offers substantial rewards for developing duplicative pharmaceuticals, which replicate the action of an existing pharmaceutical by using a similar molecule that is different enough to avoid patent infringement. Once approved, such a duplicative product can capture substantial market share from its first-in-class competitor—typically not through price competition, unfortunately, but through massive marketing efforts focused on prescribers and (where allowed) patients. Entailing only minimal improvement of our pharmaceutical arsenal, such duplicative products weaken the incentives to search for breakthroughs in areas where they would likely be quickly followed by duplicative competitors. The HIF avoids this problem by rewarding only incremental health gains—by conducting its impact assessments against a status-quo benchmark that includes the pharmaceuticals that were available when the relevant new product was developed. It thus applies different benchmarks to the two products: the impact of the breakthrough product is assessed against a benchmark that does not include its (later) copy-cat competitor, whereas the impact of the latter is assessed against a benchmark that does include the (earlier) breakthrough pharmaceutical. The duplicative product is rewarded only if and insofar as it achieves health gains that, in its absence, would not have been achieved by the earlier product. Consequently, once a pharmaceutical is registered with the HIF, there is little reason to invest in developing a duplicative product as it—whether registered or not—would earn little or no money.

These three foreseeable shifts in research priorities illustrate how, by adding the new option of rewards based on health gains achieved, the HIF would fill important funding gaps left by monopoly incentives, especially regarding vaccines and communicable diseases of poverty. It achieves such complementarity through three key differences from the conventional innovator rewards. While monopoly markup rewards implicitly value the health of people unequally depending on how much they are willing and able to pay, the HIF explicitly assigns equal value to the lives and health of all human beings. While monopoly rewards are largely insensitive to externalities, the HIF takes account of health externalities and, in particular, of how a person’s use of a pharmaceutical affects the health of other people. While current monopoly rewards treat breakthrough and duplicative pharmaceuticals symmetrically, the HIF recognizes only incremental health gains and thus discounts a duplicative product’s therapeutic benefits insofar as, in its absence, they would have been achieved by prior products anyway. Thanks to these three novelties, creation of the HIF would greatly improve the cost-effectiveness of pharmaceutical R&D.
5. How the Health Impact Fund Would Promote Access to Medicines

For the value of innovations to be realized, they must spread and be used to good effect. The HIF would ensure that all pharmaceuticals registered with it are quickly and widely accessible to those who need them. Monopoly patent rewards, by contrast, severely restrict access through the high prices that pharmaceutical companies rationally charge. The exorbitance of these markups is partly explained by existing extreme economic inequalities, both between and within countries. These lead to highly convex demand curves for important pharmaceuticals, ensuring that their profit-maximizing sales price lies far above what most patients can afford. Firms earn more by selling at a very high price to the affluent or well-insured—a mere fraction of the patient population—than by serving more patients at a lower price. Each year, millions of people suffer and die from lack of access to existing medicines that generic manufacturers would be willing and able to mass-produce quite cheaply—arguably a massive violation of the human right to health [24].

Reflecting on this tragedy, one wishes for the lowest possible price, which would make any important pharmaceutical universally affordable11 [25,26]. However, as illustrated by some very cheap generics, low retail prices can also impede access: by making it unprofitable to offer the product in small national markets and remote locations. High prices and insufficient supply incentives—the HIF avoids both problems. It caps the sales price at variable cost of manufacturing and delivery, thereby delinking it from the fixed costs of bringing new pharmaceuticals to market. However, it then supplements innovator sales revenues with health impact rewards. These supplemental payments would often make it worthwhile for innovators competently to market their registered products even below variable cost, and even in remote and impoverished areas, in order to achieve additional health gains by reaching more patients. Such efforts would be especially compelling as part of a population-level strategy aimed at suppressing the target disease. By giving even poor and hard-to-reach patients effective access to its product, the innovator prevents the disease from spreading and from evolving new strains that might not be susceptible to the innovator’s treatment.

In rewarding such innovator efforts, the HIF implements an important insight: not only is excluding poor people from the benefits of modern pharmaceuticals immoral, it is also dangerous for us all by turning low-income populations into breeding grounds for infectious diseases, which often develop new, drug-resistant strains—of tuberculosis in China and India, for instance, and of malaria in South East Asia and Ethiopia—and by rendering us unprepared for dealing with infectious disease outbreaks such as Ebola, swine flu, and COVID-19.

While, as the sofosbuvir example shows, sales prices of patented medicines often exceed 1000 times manufacturing cost, HIF-registered pharmaceuticals would be available without markup from day 1. Yet, despite their low price, innovators would nonetheless have strong incentives reliably to deliver such products, in top condition, to remote and impoverished places, with clear local-language instructions and adherence support for patients and providers. This is so because the HIF lets innovators earn more than the sales price from supplying a product. It leaves no one behind12 [27] by assigning more value to the lives and health of poor people than what they themselves can afford to pay. Doing so is morally right. It is also collectively advantageous, especially with communicable diseases, which would be central to the HIF: by containing and ideally eradicating such a disease among the poor, we protect everyone from the threat it poses, including the threat of new drug-resistant strains, which often emerge in patients who cannot afford to take an expensive drug at full dosage for the full course of treatment.

HIF-registered pharmaceuticals would truly be accessible to all who need them. Such universal access avoids large economic losses produced by monopoly markups. Because of the extreme magnitude of the gap between the retail price of patented pharmaceuticals and their variable cost of supply, the deadweight losses currently arising from this gap are likewise enormous. Most people do not buy patented pharmaceuticals at prevailing retail prices, but nearly all these non-buyers would be willing and able to buy a needed
product at some lower price above variable cost of supply. All such extra sales would be mutually beneficial to both sides. Yet the innovator must nonetheless prudently decline them in order to maintain its optimal sales price.

To illustrate, suppose that the profit-maximizing sales price of a pharmaceutical is EUR 40,000, that the variable cost of supplying it is EUR 100 and that there are 8 million buyers willing and able to pay more than EUR 100 but not the full EUR 40,000 for the product. Suppose these buyers are on average willing and able to pay up to EUR 2600 (reservation price). In this case, a foregone sale to an average buyer entails a deadweight loss of EUR 2500, consisting of a loss of $p - 100$ plus a loss of $2600 - p$ to the buyer. The aggregate deadweight loss is then EUR 20 billion. With a higher retail price, this loss increases farther as the number of untapped buyers rises above 8 million and the average reservation price is pulled up above EUR 2600 by the added untapped buyers who are willing and able to pay at least EUR 40,000.

So much for the economic analysis of impeded access: the extremely large gap between the price of patented pharmaceuticals and their variable cost of supply imposes an economic loss on the world, in the hundreds of billions each year. This substantial loss is overshadowed by the moral deadweight loss of millions suffering and even dying due to the unaffordability of important pharmaceuticals that, after having been developed, tested, and approved, could be mass-produced at very low cost. The fate of these people is a foreseen effect of our chosen method for incentivizing innovation, a method that originated in the most affluent states and was then foisted upon the rest of the world through the WTO founding treaty [28] (esp. chs. 7, 10, 20, 21) [29]. If there is a better way of rewarding pharmaceutical innovators, then we should urgently explore and implement it.

6. How the Health Impact Fund Would Affect Marketing and Exclusivity Protection

The HIF would focus registrants’ marketing efforts on achieving health gains, leading them to make all cost-effective efforts to reduce the burden of disease. Monopoly rewards, by contrast, produce strong pressures to achieve sales, regardless of their impact on health. This pressure is strong because patented pharmaceuticals are sold at extremely high prices and also because, with variable cost of supply minuscule by comparison, most sales revenue goes directly to the innovator’s bottom line. The sale of just one additional course of treatment at USD 84,000 earns the innovator nearly this amount toward recouping its R&D expenses or increasing its profit. Such enormous rewards for sales produce two powerful incentives: to make extraordinary efforts to promote sales, and to make extraordinary efforts to defend and extend the monopoly on which those exorbitant markups depend. Neither of these incentives is in the public interest.

The incentive to promote sales leads to intense efforts to persuade or otherwise induce hospitals, insurers, medical providers, and patients to use a given patented product—regardless of whether it is the best treatment for particular patients or even helpful to them at all [30,31]. As a result of such efforts, patients often end up with a treatment that has a high profit margin rather than one that is best for their health. This is especially likely because consumers are generally poorly prepared to ascertain which pharmaceutical product is best for them.

The HIF avoids this problem by rewarding innovators strictly according to how well—or poorly—a treatment works. They get no reward at all for making patients use treatments that do not work for them. In this respect, too, the HIF achieves a harmonious alignment of innovators’ financial interests with patients’ interests in good health, while monopoly rewards expose pharmaceutical innovators to temptations and suspicions of putting profits over people.

The excessive marketing efforts encouraged by monopoly rewards are not only detrimental to health, but also wasteful for innovators insofar as they often merely cancel one another out. This waste from competitive marketing is aggravated by the strong incentives that monopoly rewards provide toward developing duplicative products in lucrative markets. Once competing firms have similar patented products approved, they will engage in
competitive marketing efforts that are collectively wasteful for them. This headwind, once more, favors the proposed HIF, which would greatly reduce the share of earnings diverted to wasteful expenditures.

This conclusion is confirmed by considering exclusivity protection. Reliant on monopoly markups, innovators are extremely keen to safeguard and expand their intellectual property. They carefully patent their product in many jurisdictions, often taking out multiple overlapping patents over several years to deter possible legal challenges and to lengthen their period of effective exclusivity [32]. They scour these jurisdictions for any infringement and then go after potential and actual infringers. All these efforts around the world are expensive and diminish the rich earnings innovators derive from their sales.

Innovators’ strenuous efforts to protect their intellectual property rights never fully succeed. When patients are desperate to obtain some pharmaceutical that is priced out of their reach but known to be producible quite cheaply, then there will be agents eager to exploit the situation by manufacturing and selling, possibly under the innovator’s brand name, either illicit true copies or, more likely, fakes that do not contain the correct combination of ingredients. Such fakes are wasteful and often harmful to patients and can then also harm the innovator’s brand reputation [33]. In addition, they court the danger of drug resistance when fakes contain too little of the active ingredient. Consumption of the product then favors the more resistant pathogens by eliminating their competition, which may cause the disease to evolve new strains that are less susceptible to the active ingredient. Drug-resistant strains can also emerge, in a similar way, when patients do not complete the full course of treatment—often because of its high daily cost. By thus accelerating the evolution of drug-resistant diseases and disease strains, monopoly markups continuously erode the effectiveness of our arsenal of pharmaceuticals to the detriment of all (except perhaps shareholders of pharmaceutical innovator firms). There is no assurance at all that pharmaceutical R&D will be able to develop a new treatment for every old one that becomes inefficacious in this way.

The HIF would avoid all these problems and revolutionize motivations. HIF-registered products would typically derive most of their earnings from impact rewards rather than from their (capped) sales price. These impact rewards would encourage patentees to actively promote widespread and effective deployment of their innovation with an eye to optimizing its overall impact. They would gladly share their relevant technology and know-how to this end, even invest in subsidizing the innovation to resource-constrained buyers and in promoting optimal use, if and insofar as the increase in impact rewards gained from wider and better use is expected to exceed the cost of the relevant investments. With the genuine quality product widely available at a rock-bottom price, it is not profitable to market fake copies. Nor is it necessary to patent the product in all jurisdictions when the HIF recognizes one reputable patent as sufficient for registration.

There is one further aspect in which the HIF delivers superior efficiencies. When their earnings are tied to the health gains achieved with their product, innovators are motivated to take an interest in holistically optimizing the entire chain from bench to bedside toward the greatest feasible health gains per euro. Reducing disease with pharmaceuticals is complicated and involves many stages—from research on specific diseases and computer exploration of molecules via clinical trials all the way to enabling and motivating different patients in many countries and cultures to use a medicine to optimal effect. These stages and components of disease reduction are interdependent, posing a highly complex logistics problem. Optimization here requires not merely the solution of many disparate tasks but also harmony among solutions. Early decisions about conceiving and pursuing R&D projects should already anticipate the challenges of successful deployment: how to identify the patients who can benefit the most and, for communicable diseases, those whose timely treatment would do most to impede their spread; how to reach and treat patients in remote and impoverished locations; how to build a strong collaborative public health strategy around the product; and how to plan the worldwide suppression of the disease?
These great potential synergies suggest that the HIF would give rise to actors who can optimally run an entire operation, from R&D to delivery, though perhaps outsourcing specific subtasks such as manufacturing. Many pharmaceutical firms are well-positioned to reconfigure themselves for this expanded role. Other existing actors may also be well-positioned, such as certain NGOs, for instance, or product-development partnerships. Open to all, the HIF would, over time, bring forth pharmaceutical innovators that really excel at conceiving and executing comprehensive strategies for achieving cost-effective disease reduction.

7. How the Health Impact Fund Would Handle Health Externalities

Externalities are a transaction’s effects on third parties. In the pharmaceutical sector, communicable diseases provide the paradigm example. Appropriate treatment of patients may improve the health of other people by reducing their risk of infection. Being beneficial, these third-party effects are positive externalities. However, externalities can also be negative and occur beyond communicable diseases. For example, successful treatment of patients at high risk of heart attack may make other people less careful about their diet and exercise.

Current monopoly rewards leave externalities largely uncompensated because buyers generally do not pay much attention to effects on third parties. To be sure, as patients we may care about effects on our family and friends, but few patients reflect on how decisions about their own treatment affect the long-term incidence of their disease. Pharmaceutical firms thus have only weak financial incentives to take account of externalities in their decision making. Such weak incentives arise when patients are willing to pay a little more if a pharmaceutical does not merely make its users feel or function better, but also reduces the spread of their disease. Unfortunately, these weak incentives are offset by much stronger opposing incentives: the more a treatment reduces the incidence of its target disease, the fewer potential buyers this treatment will have in the future.

This is not a criticism of pharmaceutical firms but of their current incentives, for which citizens should collaboratively reform toward better alignment of profits with the overall health gains achieved with pharmaceuticals. The HIF would be a major step in this direction. It would disproportionately attract registrations of important new pharmaceuticals for communicable diseases concentrated among the poor, and it would take full account of the health externalities of their deployment by rewarding not merely health gains achieved for treated patients but also realized reductions in the incidence of the target disease. The latter rewards are especially sweet because such health gains are generally highly cost-effective. For example, by making its product accessible rapidly, competently, and universally in one country, an innovator may help contain an outbreak that would otherwise have spread into neighboring countries, thereby achieving health impact in those other countries without having to do any work there at all. Were its all-out effort successful in eradicating the target disease, this innovator would, without further labor, collect health impact rewards from a grateful world. The HIF would instill in pharmaceutical innovators disease curtailment and eradication as high aspirations.

By taking account of health externalities and by assigning equal value to the lives and health of all human beings regardless of their wealth and income, the HIF addresses serious gaps in the existing innovation incentives, which recent outbreaks of Ebola, swine flu, and COVID-19 have made painfully obvious: we have too little knowledge and know-how in regard to the infectious diseases of poverty, we allow low-income populations to be breeding grounds for new diseases and disease strains, and we lack incentives toward coordinated global efforts to contain, suppress, and ideally eradicate diseases. These global efforts must include poor populations: we need good, new treatments for the diseases of poverty, and we must ensure that people everywhere have access to important pharmaceuticals and can use them to optimal effect. The longer and more widely COVID-19 proliferates among the poor, the greater the probability is of nasty mutations against which our existing pharmaceuticals afford no protection. The same holds for other communicable
diseases such as tuberculosis, malaria, HIV/AIDS, and hepatitis B. The HIF includes the poor by eliciting new treatments for diseases of poverty and by ensuring that all people have access to important pharmaceuticals and know how to use them well. It would motivate innovators to build, in collaboration with national health systems, international agencies and NGOs, a strong public health strategy around their product. To earn maximum rewards, innovators would aim at supplying not many patients but—after eradicating the target disease—none at all. Monopoly rewards, by contrast, penalize such efforts: making disease eradication a financial nightmare for CEOs and shareholders: sales drop each year, then dry up completely. The HIF is needed, then, to motivate innovators to fight communicable diseases, such as COVID-19, at the population level. The absence of such incentives heretofore may well be the reason why, with all our scientific sophistication and all the trillions spent on pharmaceuticals, humanity has only ever managed to eradicate a single human disease: smallpox, which was over 40 years ago [34].

8. How the Health Impact Fund Could Be Piloted

The proposed HIF is a large agency, comparable to the World Food Program and the Global Fund. Because it works with long-term incentives, its funding must be secured for some 15 years into the future. To win governments’ support for such an ambitious undertaking, a significant pilot is essential. With funding from the European Research Council, we have concluded a small pilot in India, focused on data collection for health impact assessment [35]. The next pilot must be substantially larger and involve real rewards to innovators, showing how they respond to incentives and how much can be achieved with a given pool of reward funds.

This planned pilot would involve one single reward pool of ca. EUR 100 million, raised from governments or foundations. This is not enough to finance the full development of even a single new pharmaceutical. Instead, we would invite innovators to submit proposals of how they might, with one of their existing pharmaceuticals, achieve additional health impact in some selected low-income country or region. They might propose, for instance, to develop especially for, and then to provide in, some low-income tropical region, a heat stable or pediatric version of one of their drugs or vaccines, a fixed-dose combination, a new delivery or treatment protocol, or a suitable new diagnostic. An expert committee would select the four best proposals based on, inter alia, anticipated incremental health gains, prospects for broad, equitable access especially by the poor, susceptibility to reliable, consistent, and inexpensive health impact assessment, and promise of additional social value. Selected proponents—which might include non-commercial innovators such as DNDi and the TB Alliance—would then be given three years for implementation. Thereafter achieved health gains would be assessed—according to pre-agreed criteria, by an agency such as the IQWIG, Deval, or the Institute for Health Metrics and Evaluation—and the reward pool be divided proportionately.

The pilot would show concretely how pharmaceutical innovators respond to the novel competitive impact rewards and how health impact can be assessed in a reliable and timely manner. It would help refine impact assessment and provide an indication of the cost-effectiveness of competitive impact rewards. With a successful pilot, an international agreement to establish the HIF would become a real possibility. In addition, the HIF pilot would yield its own substantial health gains and health policy insights through the pilot projects it monitors and rewards.

9. Conclusion

We share responsibility for what our governments, severally or in concert, decide in our names. The current international rules governing pharmaceuticals use monopolies to promote innovation. This regime systematically excludes the poor—most obviously by making advanced patented pharmaceuticals unaffordable to them, even while these can be generically mass-produced quite cheaply. This exclusion supports a serious challenge to the justice of the existing regime.
Defenders of the status quo appeal to the human right to “the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author” (Universal Declaration of Human Rights, Article 27, echoed in the International Covenant on Economic, Social and Cultural Rights, Article 15.1(c)). Such defenders also point out that costly and risky attempts at innovations would rarely occur if innovators did not have fair prospects of recovering their investment and making appropriate profits.

The present essay shows how we can respect these two points and still dramatically reduce the horrifying exclusion of the poor. The Health Impact Fund would ensure that pharmaceutical innovations are amply incentivized and rewarded while giving equal weight to the lives and health of all human beings, regardless of their socio-economic position.

The HIF improves upon innovation prizes and other pull mechanisms—such as advance market commitments\textsuperscript{16} [36,37]—in five ways. It constitutes a structural reform, establishing stable and predictable long-term innovation incentives. It lets innovators, who know their own capabilities best, decide which innovations to pursue across the whole range of disease areas. It avoids having to specify a precise “finish line”—hard to get right in advance—and instead rewards each registered innovation according to the benefits produced with its deployments. It avoids having to specify a reward-for-benefit rate, which instead evolves endogenously through market forces. It gives innovators strong incentives to also promote (through information, training, technical assistance, discounts, etc.) the fast, wide, impactful diffusion of their participating innovations.

Creating the HIF would be an extremely cost-effective reform, potentially freeing millions of mostly poor people from their debilitating ailments and greatly improving humanity’s preparedness against communicable diseases. In fact, its true cost is likely to be markedly negative insofar as savings on registered pharmaceuticals and other healthcare costs as well as gains in economic productivity and associated tax revenues would benefit the contributing funders—directly, and also indirectly by reducing the cost of health insurance, national health systems, and foreign aid. In addition, the HIF largely avoids the wasteful expenditures now typical of the pharmaceutical sector: expenses for multiple staggered patenting in many jurisdictions with associated gaming efforts (e.g., evergreening), costs of searching and preventing monopoly infringements, costs of mutually offsetting competitive promotion efforts, economic deadweight losses, and costs due to corrupt marketing practices and counterfeiting. Thanks to these astounding inefficiencies of monopoly rewards, a shift toward impact rewards could dramatically improve global health and the lives of the poor without cost to anyone, thereby producing a triple win: for the potential beneficiaries of innovative pharmaceuticals, for pharmaceutical innovators, and also for governments and taxpayers.

More fully including the poor in the benefits of pharmaceutical innovation is an imperative of justice and strongly supported by prevailing international commitments as enshrined, for example, in the Universal Declaration of Human Rights: “Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care . . . ” (Article 25), in the International Covenant on Economic, Social and Cultural Rights, recognizing “the right of everyone to the enjoyment of the highest attainable standard of physical and mental health” (Article 12), and in the Sustainable Development Goals, especially “Goal 3. Ensure healthy lives and promote well-being for all at all ages” with its associated targets to “reduce the global maternal mortality ratio” (3.1), to “end preventable deaths of newborns and children under 5 years of age” (3.2), to “end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases” (3.3), to “achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all” (3.8), to “support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines . . . for all” (3b), and to “strengthen the capacity of all countries,
in particular developing countries, for early warning, risk reduction and management of national and global health risks” (3d) [38]. The HIF would be highly effective at promoting all these rights and targets.

Pharmaceuticals are among humanity’s greatest achievements. They have helped attain dramatic improvements in health and longevity as well as significant cost savings through reduced sick days and hospitalizations. With the addition of the proposed Health Impact Fund, the pharmaceutical sector could contribute even much more—with financial net gains to innovators and the public. The dark disaster of COVID-19 might yet give rise to a new dawn of massive progress in human health.

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Notes

1 For 2019, Our World in Data reports 2.49 million deaths from pneumonia (https://ourworldindata.org/pneumonia) as well as 1.53 million deaths from diarrheal diseases, 1.18 million deaths from tuberculosis, 643,000 deaths from malaria, and 79,000 deaths from hepatitis (https://ourworldindata.org/causes-of-death). [8,9]

2 https://www.fao.org/worldfoodsituation/foodpricesindex/en/. [10] The world food price index stood at 95.1 in 2019 and at 157.4 in May 2022.

3 2.2 billion human beings lack safe drinking water, http://www.who.int/news-room/fact-sheets/detail/drinking-water. [12]

4 2 billion people live without adequate sanitation, https://www.who.int/en/news-room/fact-sheets/detail/sanitation. [13]

5 Well over 1 billion people lack adequate housing. UN Habitat, Fact Sheet 21: The Right to Adequate Housing (https://www.ohchr.org/documents/publications/fs21_rev_1_housing_en.pdf), p. 1. [14]

6 940 million people have no electricity, https://ourworldindata.org/energy-access. [15]

7 Some 160 million children aged 5-17 do wage work outside their own household and hence do not go to school (https://www.ilo.org/ipec/Informationresources/WCMS_800278/lang--en/index.htm) and over 750 million adults are illiterate (https://en.unesco.org/themes/literacy). [16,17]

8 Since then, Africa’s share of world population has risen to 17%.

9 For the Health Impact Fund project website, see https://healthimpactfund.org/en/. [21]

10 For some initial work toward conceiving a Green Impact Fund for Technology, see https://globaljustice.yale.edu/green-impact-fund-technology. [22]

11 This wish manifests itself in frequent calls for compulsory licensing, as permitted under Section 5 of the Doha Declaration, https://www.wto.org/english/thewto_e/minist_e/min01_e/min01_e.htm. [25] With a compulsory license, a government overrides a national patent by authorizing a firm within its jurisdiction to manufacture and sell the patented product there while paying the patentee a small share of its earnings. So constrained, compulsory licenses can bring relief only in countries with adequate manufacturing capacity. Such licenses are strongly discouraged and penalized by the U.S. and therefore rarely used. For the pressure the U.S. applies and many hostile references to compulsory licensing, see the Special 301 Reports published by the Office of the United States Trade Representative (https://ustr.gov/issue-areas/intellectual-property/Special-301). [26]

12 This maxim is a key idea animating the Sustainable Development Goals. See UN Sustainable Development Group, “Leave No One Behind,” https://unsdg.un.org/2030-agenda/universal-values/leave-no-one-behind. [27]

13 Because the deadweight loss is the sum of the two losses, the price $P$ ($100 < P < 2600$) at which the foregone sale might have been consummated is irrelevant to calculating its magnitude.

14 This loss cannot be quantified precisely because, for most of the excluded potential buyers, the reservation price is unknown.

15 A well-known example is the opioid crisis festering in the United States since 1999, causing a record 108,000 deaths in 2021 (https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm). [30] Another well-known case is the Vioxx scandal, where Merck left a highly profitable drug on the market even while knowing its tendency to cause strokes and heart attacks. According to an internal U.S. Food and Drug Administration study, Vioxx is estimated to have caused tens of thousands of premature deaths in the United States (http://www.sefap.it/farmacovigilanza_news_200501/FDA%20vioxx.pdf). [31]

16 See Michael Kremer and Rachel Glennerster. Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases (Princeton: Princeton University 2004); [36] and Michael Kremer, Jonathan Levin, and Christopher M. Snyder. “Designing
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