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Publicly Funded Clinical Trials: A Route to Sustained Innovation with Affordable Drugs

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Abstract

The current system of financing pharmaceutical research through patent monopolies or other forms of market exclusivity is fundamentally flawed. It creates an altogether unnecessary problem by making drugs that are cheap to produce extremely expensive to the patients who need them. The fact that most of the cost is borne by third party payers undermines the traditional argument for market prices as conveying information about households' desires. This system of pricing also leads to the sort of waste and corruption that would be predicted from a system in which government granted monopolies lead to items being sold at prices that are typically several thousand percent above their cost of production.

This proposal outlines a plan for a pilot project of public financed clinical trials. Under this proposal, government(s) would set aside a limited amount of funding to finance clinical trials and bring drugs through national approval processes. This funding would be awarded under long-term contracts (8–10) years on a competitive basis. The winners of the contracts would test promising compounds of their choosing in the areas where they have designated an interest. As a condition of getting the funding, all the results of the tests will be fully available to the public. In addition, whatever drugs are approved would have no exclusivity conditions, so they could be sold as generics.

In addition to making potentially important new drugs available to the public, this pilot will set a model for transparency in research. The practice of disclosing all test results in a timely manner should pressure other pharmaceutical companies to adopt the same practice. In addition, since the contracts and the number of trials will all be public information, this project will also provide substantial insights into the cost of clinical trials and drug development.

Introduction

The current system of financing research through patents and other forms of exclusivity suffers from all the problems that would be predicted when the government enforces monopolies that raise prices by several thousand percent above their free market price. In addition to the difficulties that high prices create for patients and/or government health services, they also lead to the sorts of waste, abuse, and corruption economic theory predicts.

This proposal is designed to test the merits of an alternative mechanism for supporting the development of drugs. Under the proposal, a government, group of governments, or non-governmental body would set aside a sum of money to finance the clinical tests of promising compounds. This money would be awarded through long-term contracts (8−10 years), issued on a competitive basis, to pharmaceutical companies or non-profit organizations, that developed plans to test compounds in particular disease areas.

Since a major goal of the pilot is to promote transparency throughout the industry, there will be explicit conditions attached to the awarding of the contracts:

1) The protocols for the clinical trials would be publicly available;
2) All results from the trials would be publicly available, with as much patient-level data disclosed as is consistent with preserving anonymity;
3) Tests should include not only new products, but also new regimens (combinations, different doses, etc.)
4) All the outcomes of the tests will be fully available to the public and other producers. This means that rights to test data will be freely available so that all drugs developed through this process can be immediately sold as generics.

The conduct of contractors would be subject to regular review to ensure that tests are being carried through in an ethical manner. Assuming a continuing stream of funding, contracts will be renewed and/or expanded based on the extent to which a contractor can show that their work contributed to public health. Under plausible scenarios the reduction in drug prices and gains to public health should easily exceed the cost of this project.

Publicly Funded Clinical Trials: An Outline

The rationale for a system of publicly funded research trials is to circumvent the need to recover research costs with high drug prices by directly financing the clinical trial portion of the research process. The clinical testing process likely accounts for the bulk of privately funded drug research, although the exact division is difficult to know since the industry does not provide breakdowns of its research expenditures. It is also the portion of the process where conflicts of interest and concerns about misrepresentations of data provide the greatest grounds for concern.[1]

Clinical testing is also the portion of the process that most easily lends itself to public oversight. A clinical trial is a reasonably well-defined product, in which there are clear guidelines for phase 1, phase 2, and phase 3 trials. It is much easier to determine whether these guidelines are being followed in testing than whether pre-clinical research is following a useful path. For these reasons, it is appropriate to target the clinical testing portion of the process for public funding.

While an ideal system may entirely rely on publicly funded clinical trials, it is necessary to establish the potential benefits of going this route on a more limited basis. This could be done by committing a limited pool of funding to support a set of publicly funded clinical trials in one or more areas, such as cancer research.

The strategy would be for the funding to be awarded to private pharmaceutical companies or non-profit organizations, on a competitive basis. The funding would take the form of multi-year contracts (e.g. 8−10 years), which would allow the recipients adequate time to demonstrate the importance of their work. The bidders would indicate a general plan for conducting tests in a particular area, and not commit themselves in advance to a specific set of tests. This would give them the flexibility needed to alter their plans based on their own results and other research. The contractors would also be responsible for getting drugs through the drug approval process in at least some countries. The contracts would be subject to renewal and/or expansion (pending funding) with the major determinant being the ability of the contractors to demonstrate that their work had advanced public health.

1 If findings at the preclinical stage are misrepresented, this should be exposed in the clinical tests. This could lead to wasted spending, and some needless risk to people involved in clinical trials, but there would be no large-scale threat to public health, as would be the case if results in clinical trials are misrepresented.

The contracts would be attached to a series of conditions.

1) The test protocols and results would be fully available to the public. This means that the protocols should be available at the time the testing begins. The results of tests should be posted on a website on an ongoing basis, with as much patient-level data disclosed as is consistent with preserving anonymity. The goal should be to have a data set that would allow any interested researcher to have the same ability to analyze the data as the company that carried through the research.

2) All the results, including patents and data and marketing rights gains by these firms, would be available to the public on a copyleft basis.[2] This means that any drugs developed through this process could be sold as generics immediately after approval. In cases where a contractor opted to test a compound that was still subject to patent protection they would be responsible for purchasing the rights so that it could be sold as a generic once the approval process is completed.

3) The testing process itself would be subject to regular review to ensure that it is meeting accepted ethical standards, such as proper patient consent. Failure to meet standards would a basis for forfeiting a contract.

The benefit of contracting out the process of choosing compounds and conducting the testing is that it removes the need for a government agency to micro-manage the process and also limits concerns about political interference. The public's interest in openness and well-conducted trials, as well as open access to the fruits of the testing, is assured by the conditions of the contracts.

In carrying through their work, the contractors would first need to determine which compounds merit testing. There are a vast number of compounds already in the public domain, so for many drugs they may want to test there would be no issue of patent rights.[3] However, there are many

2 "Copyleft" refers to a type of copyright that came out of the Free Software movement. It allows anyone to use the protected material, as long as what they use it in is left in the public domain. If a user wants to get a copyright for material that includes work that is subject to copyleft rules, then they must negotiate with the holder of the original copyright. In the case of patents, this would mean that other researchers or pharmaceutical companies could take advantage of any patents held by publicly funding contractors, as long as they put the products of their research in the public domain. If they wanted to use this research to develop a product in which they held a patent or used a form of marketing exclusivity for private gain, they would have to negotiate this opportunity with the testing company. Except in extraordinary circumstances, the regulations should be structured so that such deals are not an option.

3 Only 15 percent of the new drug approvals in the United States from 2004−2014 involved new chemical entities.

newly developed compounds that offer promising treatments. In these cases, the contractors would need to buy the patent rights before they proceeded with testing. In such cases, they would effectively be bidding against competitors that are relying on patent rents to cover their research costs.

Presumably contractors that expected to be testing new compounds would incorporate the projected price for buying patent rights in their bids. In subsequently making the case for a renewal or expansion of the contract they would have to be prepared to show how the health benefits from a new compound warranted the additional expense, since the cost would mean they would be able to perform fewer clinical tests than their competitors.
On the other side, by buying up a patent and placing it in the public domain, they will have opened up an area for testing by other researchers as well. If a contractor's tests with a patented compound proved unsuccessful, but another contractor was able to successfully use the compound to treat another condition, then the purchase will still have advanced public health. This would be the sort of issue that should be taken into account in determining whether a contract is renewed.

A major difference between the outcome when a publicly funded contractor gains control of the patent and when a private pharmaceutical company has control is that in the former case the patent would be placed in the public domain. This would allow others to benefit from the patent, which could mean experimenting with their own clinical trials based on the compound. However, since the patent is subject to copyleft rules, any competitor who successfully tests the drug and gets it approved for use would also be required to make it available as a generic. In other words, they could not have monopoly rights on the test results, if they used a patent that had been purchased by a publicly funded contractor.

There is an enormous range of estimates on the cost of clinical trials. At the low end, there is data from the Drugs for Neglected Diseases Initiative (DNDI) reporting the combined cost of Phase II and Phase III trials at less than $20 million (DNDI, 2014). At the high end, DiMasi et al. (2014) report the average cost of Phase I, Phase II and Phase III trials at $36.5 million, $56.4 million, and $86.3 million (in 2013 dollars), respectively.[4] The DNDI numbers do not include the value of in kind contributions from partner companies. Including the value of these contributions would raise the costs by at least 20 percent, according to an estimate from DNDI, and possibly by considerably more. However two factors that kept costs low are that the tests were conducted in developing countries and also the tests were being conducted on qualitatively new treatments. The latter factor

4 DiMasi et al. relies on proprietary data from the pharmaceutical industry, which has an incentive to make its costs appear as high as possible to justify high drug prices. For this reason, the data should be viewed with caution and treated as almost certainly being a high-end estimate of the actual costs.

meant that a large sample size was not necessary to find a statistically significant effect. By contrast, if the drug being tested is intended to treat a condition for which one or more effective drugs already exist, it may be necessary to have a very large sample in order to demonstrate a statistically significant improvement in outcomes.

From the standpoint of advancing public health, resources would generally be much better devoted to developing drugs for conditions where no effective treatments exist rather than developing drugs that largely duplicate the function of existing drugs. For this reason, the differences in the cost of the clinical trials would give the right incentives to contractors, in addition to the fact that the development of duplicative drugs would provide much less basis for renewing contracts than the development of breakthrough drugs.

The extraordinary gap between these estimates of developing costs makes it difficult to determine an appropriate level of funding for a pilot project. Ideally, the project should be large enough to produce a reasonable number of successful drugs over a relatively limited time horizon. If the target is 5 to 10 successful drugs over ten years, this could imply total costs as low as $100 million to $200 million using the DNDI estimates. By contrast, the DiMasi et al. estimates would imply costs of between $5.7 billion and $11.4 billion, assuming no new chemical compounds are used.[5] Both figures are over a 10-year horizon, so annual costs with the DNDI estimates would be between $10 million and $20 million, with the DiMasi estimate annual costs would be between $570 million and $1.14 billion.

Even using the DiMasi figures, it is likely that a pilot project could provide savings and public health benefits that would vastly exceed its costs. If the pilot produced just one moderately successful drug (measured in sales volume) the savings could easily exceed $900 million annually.[6] In addition, if the drugs developed primarily benefit people in developing countries, the public health value might vastly exceed the monetary savings in a counterfactual situation.

In addition, the public will benefit from having open research that other researchers could use, as well as doctors and patients. The clinical trials can have patient-level data publicly available in the same way that economists make survey data available for general use. The data would show the baseline characteristics for all the patients in the tests. This would make it possible to determine the

5 These numbers do not include a cost of capital, which accounts for a large portion of DiMasi's cost estimate. This exclusion is appropriate since contractors are presumably being paid on an ongoing basis, so they are not risking their own capital.

6 This assumes sales volume of $1 billion annually for a moderately successful patent protected drug and that the generic version would sell for one-tenth of the price.

relative merits of the drugs for people with specific characteristics, such as distinctions based on gender or age, various health conditions, and interactions with other medicines.

Making this information publicly available could become a standard that would be adopted in testing more generally, even in tests that are not conducted by government contractors. This would lead to better treatment, as doctors could make more informed decisions in prescribing medicine. It would also make it more difficult for drug companies to misrepresent research findings. And, it would pave the way for more productive future research, as gaps in treatment would be more apparent.

In sum, the necessary outlays to carry through a limited number of clinical trials are relatively modest compared with current research spending and a trivial relative to the size of total health care spending. Even with modest assumptions on success, the costs should easily be recovered through lower government payments for prescription drugs, as well as reduced tax subsidies to individuals for private expenditures. In addition, this route should allow for better treatment and more effective research since all the findings could be made public for researchers, doctors, and patients could use it. If a limited test of publicly funded clinical trials proved successful, there would likely be public support for adopting this path more generally and applying it to all areas of pharmaceutical research.

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