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Can transferable patent extensions solve the market failure for antibiotics?

by Pierre Dubois, Paul-Henri Moisson & Jean Tirole

Economics for the Common Good

Can transferable patent extensions solve the market failure for antibiotics?

Antibiotic resistance is a serious global public health problem, and has been a growing threat since the 2000s. The costs are significant, both in terms of human lives and the financial cost of care to society. Health care systems have not been able to provide sufficient financial incentives for innovation against antimicrobial resistance. This is why, within the framework of the TSE Health Center and the ARPEGE project, TSE's research aims to identify new economic models adapted to innovations developed in the antimicrobial resistance sector. Building on a working paper[1] prepared Pierre Dubois, Paul-Henri Moisson and Jean Tirole, this policy paper highlights the mechanisms and levers to be used to encourage innovation.

The shortage of new antibiotics in the pipeline raises the possibility of a new pandemic, of the bacterial kind this time. What is your take on this? Why does the patent system not suffice to provide the proper incentives for antimicrobial R&D?

First, of course, there have been many calls for more stewardship to limit the growth of resistance. There is a vast overconsumption of antibiotics by humans and animals. Second, and regardless of the success of stewardship policies, new antibiotics must be discovered. The problem is that there does not seem to be a business model. A new antibiotic brings limited value whenever existing antibiotics still work. In contrast, it can easily be lifesaving as an "antibiotic of last resort", with a very high social value then.

In a nutshell, stewardship calls for a minimal usage of new antibiotics. Their therapeutic value is however often computed in comparison with existing antibiotics, thereby underestimating their lifesaving benefits and their dynamic value against antimicrobial resistance.

Is this the only therapeutic class for which stronger pull mechanisms are required?

Not really. Small patient numbers (orphan diseases), patients' limited ability to pay (drugs for LDCs), and externalities (vaccines, and of course antibiotics) all create a wedge between the social and private values of pharmaceutical innovations and motivate a different approach. The standard business model, based on intellectual property, is broken for such innovations.

1. Working paper N°1377, "The Economics of Transferable Patent Extensions", November 2022.

About the ARPEGE project

ARPEGE, a French multidisciplinary consortium led by the French biotech Antabio and conducted jointly with bioMérieux, the Hospices Civils de Lyon and TSE, aims to develop a set of solutions designed to strengthen the capacity of healthcare institutions to fight antibiotic resistance. To develop this project, the consortium has received public funding under the "PSPC" call for projects operated on behalf of the French government by Bpifrance as part of the 'investments for the future' program (PIA).

ARPEGE is the french acronym for economic, diagnostic and therapeutic approach to antibiotic resistance. This pioneering project combines preventive, diagnostic, therapeutic and economic approaches, thus aiming to provide a multidisciplinary solution to the problem of antibiotic resistance. It is of major importance for public health, structuring innovation capacities and strengthening health systems through an innovative model.

Is that why Sweden and the UK have offered cash prizes to address the shortage of antibiotics?

For centuries, the alternative approach to intellectual property has been the granting of cash prizes, or in their modern form advanced market commitments, following up on the work of economics Nobel laureate Michael Kremer. The idea is to reward the innovator in cash and put the innovation in the public domain so as to allow maximal diffusion. Two comments here:

- First, if Sweden and the UK are indeed taking the cash reward approach, pandemics are global ills. Country-specific policies are best designed at the international level, as most countries by themselves are too small. Indeed, Sweden and the UK are not willing to spend what it takes to generate interest in antibiotics research. To be certain, international agreements are hard to design because of the individual countries' temptation to "free ride", as the climate change global mismanagement amply demonstrates. Another branch of our research actually shows the difficulty in building R&D coalitions when holdouts can enjoy the benefits of licenses once others have invested.
- Second, and more to the point for our current research, while reinforced pull mechanisms usually take the form of prizes, it has lately been proposed that inventors of new antibiotics be rewarded with an original "currency": transferable exclusivity extensions (TEEs) or "vouchers". The inventor would be given a patent extension right of a given duration, and this right could be either used by the inventor itself or, more likely, be sold by the inventor to an entity with an existing IP right, that would then enjoy the extra period of exclusivity after the normal patent protection expiration date.

Our research thus focuses on the second challenge: for a given reward for the inventor, how should one structure its delivery at the least cost for consumers/taxpayers? Is a cash transfer or a voucher system better?

What was your initial reaction to this voucher scheme?

A cautious one. We understood that in Europe the voucher scheme could bypass some of the difficulties associated with the budgetary process. The free-rider issue just mentioned might prevent any such joint budgetary action. In contrast, the European Medicine Agency can delay the entry of generics for the molecule that has purchased the voucher, for a period equal to the length of the voucher, de facto enforcing the IP rights associated with the voucher.

The reason for being wary was two-fold. To understand this, recall that providing innovators with strong incentives while protecting consumers/taxpayers has always involved a complex trade-off between, first, rewarding inventors in proportion with their contribution to society, and second, structuring the reward at the least cost for consumers/taxpayers.

Let's start with the question of commensurability of the reward with the social value of the antibiotic…

A voucher system may involve both an uncertainty about how much money would be granted to the discoverer of a new antibiotic and a concern about whether this amount over- or under-rewards the innovation.

- A pre-specified duration (say, a year) for a voucher creates uncertainty about the exact reward accruing to the antibiotic developer, as well as the overall costs incurred by patients and taxpayers, which raises concerns. We realized, though, that the uncertainty can be eliminated by letting the voucher's potential buyers bid in terms of extension length.

  Namely, fix an arbitrary $ reward for the antibiotic developer. And let the buyers announce the minimum length for the voucher that makes them willing to pay this amount of money for the right to extend their patent by this length[2]. The winner of the voucher auction is the buyer who specifies the lowest length . The uncertainty about the reward is gone.
- The question of the level of reward (is the reward set at the appropriate level?) arises whether a prize or a voucher mechanism is selected. In the end, the answer hinges on a proper assessment of the therapeutic value of the new antibiotic. While the economist can bring a few elements of methodology, the assessment is primarily one of public health.

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You said that you were initially concerned about the voucher system…

At first sight, vouchers, which prolong monopoly distortions, would seem to be dominated by prizes, which do not. This however ignores two considerations. First, cash transfers must be financed from the general revenue, engendering a shadow cost of taxation; tax collection distorts economic incentives and therefore $1 in public expenditures usually costs more than $1 to society (which does not mean that public expenditures are wasteful, because their benefit may well be even higher). A commonly used number for developed countries is that $1 of taxes costs $1.3, a 30% deadweight loss; but such a number is only an indication; deadweight losses are specific to the country (efficacy of tax collections, social norms in evading or optimizing on taxes, and more generally "elasticities of supply") and on the specific tax that is being employed.

2. *A maximum length can/should be specified by the auction designer.*

Second, and the novelty of this paper, the benefits of prizes are often overestimated, at least in the absence of a tight intervention into the production and delivery process. The generics experience demonstrates that when the knowledge underlying the branded drug falls into the public domain, prices remain far from competitive for multiple reasons: single supplier of generics or multiple colluding ones, consumer attachment to the branded product, existing regulation. Imperfect generics competition is of particular interest here, as it implies that ending the exclusivity of the branded drug operates a transfer away from the originator, that is detrimental to the incentive to innovate without any corresponding benefit for the consumer. Indeed, if generics were competitive, a reward of $1 would imply a loss of consumer surplus greater than $1. A striking conclusion of our empirical work however is that an incentive reward of $1 through a European voucher system would cost less to the consumer than $1 (and a fortiori less than the cost of a cash award of $1) in most of the European countries in our data set!

How do you compute the cost of rewards through the voucher system?

Our theoretical work computes the cost-over-reward ratio of a TEE scheme for a flexible class of demand functions for the molecule that will benefit from the patent extension (the winner of the voucher auction). We take into account the existence of regulation of the branded molecule during and after the exclusivity period.

This ratio is independent of the market size for the molecule and the share of captive consumers for the originator at the end of the exclusivity period, decreases with the generics' price at the end of the exclusivity period, decreases with the regulator's bargaining power, and increases with the marginal cost of production.

That is for a given country. What about unions?

Coalitions of countries are needed to provide enough financing, as we argued. Within a union (such as the United States or Europe), decisions are made through majority or supermajority (or even unanimity) voting. It is therefore important to compute the impact of a cash transfer or a voucher scheme on the various polities. This requires making some assumptions on how cash is levied in the case of a prize (for Europe we assume that contributions to the European budget are proportional to country income).

It is also important to understand the differentiation of the impact of a TEE on member countries or states. The theoretical prediction is that a union member tends to prefer a TEE scheme over a cash transfer scheme if:

- Its generics prices are high and the market share of generics low (such a country suffers less from a TEE)
- Its cost of public funds is high (such a country finds cash transfers more costly),
- The drug with extended exclusivity has a relatively low (per inhabitant) market in the country (say, an anti-cholesterol treatment faces less demand in Greece than in Finland).

To go further, though, one must delve into the empirical analysis, building on the theoretical modeling.

Interestingly, we obtained that almost all countries should prefer a voucher system to a cash levy proportional to their GDP, even though a few are reluctant given their specific preferences.

Can you explain your empirical strategy for a layperson?

We use data on fifteen European countries (including France, Germany, Italy and Spain)' expenditures and quantities by drug to calibrate our theoretical model and obtain an estimation of the cost-over-reward ratio of a voucher for each country. The data allow us to infer each country's demand levels and price elasticities, which matter for the consumer surplus losses associated with an exclusivity extension. We recover from the data the level of regulated prices under exclusivity and after generics entry. Using these country-specific data and estimations, we compute the cost-over-reward ratio for each single country, either in isolation or in a union, and compare it to standard values of marginal costs of public funds. These calculations should inform decision makers about the benefit of a voucher system over a cash transfer. Interestingly, we obtained that almost all countries should prefer a voucher system to a cash levy proportional to their GDP, even though a few are reluctant given their specific preferences.

How do you explain the country-specific preferences?

Country specific preferences are not surprising: The health care institutions, the demography and epidemiology, the income per inhabitant and the regulatory policies concerning generics pricing and substitution all differ across countries. Our theoretical model shows that countries with higher levels of generics penetration and/or lower prices of generics should be relatively less favorable to a voucher system, but that the preferences over a cash transfer depend in a complex way on the price sensitivity of demand for drugs in each country.

Would you conclude that a voucher system is desirable in Europe?

The design of such policies is complex, and we addressed only their economic aspects. Even from a strict economic perspective, a strong market power in the voucher market or a strong aversion to uncertainty regarding the length of exclusivity extensions (from hospitals and generics makers in particular) may significantly reduce the desirability of a voucher system in practice. However, legal aspects are also important to address concerning the ability of the EMA to enforce exclusivity extensions. From this perspective, it seems such a system has benefits both in terms of political economy (avoiding the freeriding problem of cash, it helps reach agreement among European countries) and in terms of efficiency of state spending.

This research is the first analysis of the relative costs and benefits of two enhanced pull mechanisms: prizes and vouchers. The conclusions are necessarily tentative, and the results will need to be confirmed using other data sets. Furthermore, and as other researchers have pointed out before us, details of a voucher scheme must be paid attention to. Legal concerns about the ability of the EMA to enforce exclusivity extensions should be assuaged. Generics makers have to be warned in advance of the existence of a TEE, which implies that potential buyers' patents that are meant to benefit from the voucher should not be too close to expiration.

Subject to these caveats, the voucher system has benefits both in terms of political economy (avoiding the free riding problem of cash, it helps reach agreement among European countries) and in terms of efficiency of public spending. This latter aspect was an eye opener for us. Prolonging the monopoly distortion on existing drugs a priori did not seem appealing. However, part of the originator's loss in profit when exclusivity ends slips through the cracks (generics' entry costs, generics' profits) and do not benefit the consumers. This redistribution implies that the shadow cost of raising a $1 for the inventor can be less than $1. Our empirical analysis shows that this is not a theoretical curiosum and that TEEs are well worth considering.

SUMMING UP

- The conjunction of stewardship policies aimed at fighting antimicrobial resistance, and inadequate therapeutical value assessment has deterred R&D investment in innovative antimicrobials. **Our society needs to solve the broken market incentives problem in order to avoid a future microbial pandemic.**
- **The revenues of innovative antimicrobials must be delinked from the sales quantities to accommodate both stewardship and incentives for antimicrobial innovation**. However, given the scale of the required R&D investments, no single country can provide strong enough incentives by itself. Unfortunately, international agreements are hard to design because of each country's temptation to "free ride" on the others' contributions and efforts, as the climate change global mismanagement and inaction amply demonstrates.
- **A voucher system of Transferable Exclusivity Extensions (TEE) provides an original "currency" with which to reward inventors:** The inventor of an innovative drug would be given a patent extension right, and this right could be sold to an entity with an existing IP right, that would then enjoy the extra period of exclusivity after the standard patent protection expiration date.
- Because of the uncertainty as to the vouchers' market value, **TEEs should not be awarded with a given duration, but rather with a fixed "value".** Potential voucher buyers would then bid for the lowest duration for which they are willing to pay the "value".
- Implemented by the European Medical Agency across its member states, **a TEE scheme would not only solve the free riding problem at the European level, but also, as our empirical results suggest, may be preferable to a union-wide cash transfer (prize) in terms of social costs.** The reason is that a longer exclusivity period redistributes some of the generics' rents post-exclusivity to the original patent owner (such rents tend to be large in most countries as generics' prices largely exceed their marginal costs). The relative desirability of TEEs with respect to cash transfers is even stronger if the in-efficiency of tax collection and the concomitant cost of raising public funds are taken into account.

About the authors

Antibiotic resistance is a major societal problem, and my colleagues and I are delighted to put forth economics towards project ARPEGE to propose long-term solutions to improve global health.
Jean Tirole

Pierre Dubois *is Professor of Economics at TSE, fellow of the CEPR and of the Institute for Fiscal Studies in London, senior member of Institut Universitaire de France and TSE Health Center's Director. He has been assistant professor at the University of Montréal, has held visiting positions at Berkeley, Northwestern University and Harvard University. He has also been Scientific Director of TSE and is currently co-editor of the Journal of the European Economic Association.*

His work includes research on industrial organization, health and pharmaceuticals, food demand and applied econometrics.

Paul-Henri Moisson *is a PhD student at TSE. He graduated from Ecole polytechnique. His fields of predilection are organizational economics, political economy and industrial organization. His thesis advisor is Professor Jean Tirole.*

Jean Tirole *is honorary chairman of the Jean-Jacques Laffont Foundation (TSE) and IAST, and scientific director of TSE-Partnership. He is also affiliated with MIT, where he holds a visiting position, and the Institut de France.*

He is laureate of numerous international distinctions, including the 2007 CNRS gold medal and the 2014 Sveriges Riksbank prize in economic sciences in memory of Alfred Nobel.

Professor Tirole's research covers industrial organization, regulation, finance, macroeconomics and banking, as well as psychology-based economics. His work in health economics today focuses on the source of market failures for the innovation in antibiotics as well as the regulation and ethics of digital technologies in health care.

TSE expertise in the field of health economics

The Toulouse School of Economics (TSE) aims to undertake research that helps organizations in both the public and the private sector to address health issues and improve quality and access to care both in France and worldwide. For more than a decade, TSE economists have been studying such diverse topics as healthcare, innovation, ageing, pharmaceutical regulation, food and nutrition issues. The set of questions and problems for economists is huge. Researchers in economics can develop and use new tools to address questions of regulation and organization of healthcare and innovation.

In 2021, TSE expanded its footprint in this area by creating a Health Center aiming at developing research of excellence in the field of health economics. Combining TSE's own expertise with its private and public partners' financial support and knowledge, TSE Health Center supports a variety of research work in the field of health economics.

Research focuses

- Pharmaceutical industry and regulation
- Innovation in health
- Public healthcare, long term care and aging
- Food and healthy behavior economics
- Economics of pandemics

TSE Health Center gather more than 30 researchers from various background. TSE researchers are at the origin of many scientific publications, particularly in the field of antibiotic economics.

Our partners contribute to the scientific activities of TSE Health Center. Their support is essential to help TSE Health Center become one of the best research centers focused on health economics.

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