

# Advance price or purchase commitments to create markets for treatments for diseases of poverty: lessons from three policies

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**Abstract** New drugs and vaccines are needed for tackling diseases of poverty in low- and middle-income countries. The lack of effective demand or market for these products translates into insufficient investment being made in research and development to meet the need for them. Many have advocated cost-reducing (push) and market-enhancing (pull) incentives to tackle this problem. Advance price or purchase commitments (APPCs) funded by international agencies and governments offer one way forward. This paper looks at design issues for APPCs for drugs and vaccines for diseases of poverty drawing on experience and lessons from three case studies: the introduction of the meningitis C vaccine in the United Kingdom; the Orphan Drug Act (ODA) in the United States of America (US); and the newly legislated US Project BioShield for bioterrorist interventions. Our key conclusion is that APPCs have the potential to be a powerful tool and should be tried. The correct structure and design may only be determined through the process of taking action to set one up.

**Keywords** Orphan drug production/economics; Motivation; Drug costs; Prospective payment system; Contract services; Research support/economics; Poverty; Case reports (*source: MeSH, NLM*).

**Mots clés** Médicament orphelin/économie, Motivation; Coût médicament; Système remboursement (USA); Service contractuel; Aide recherche/économie; Pauvreté; Étude de cas (*source: MeSH, INSERM*).

**Palabras clave** Producción de medicamentos sin interés comercial/economía; Motivación; Costos en drogas; Sistema de pago prospectivo; Servicios contratados; Apoyo a la investigación/economía; Pobreza; Casos clínicos (*fuentes: DeCS, BIREME*).

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## Introduction

Diseases of poverty are diseases such as malaria, tuberculosis, leishmaniasis, African trypanosomiasis, dengue, Chagas disease and schistosomiasis that predominantly afflict poor populations in low- and middle-income countries (1). This paper focuses on one mechanism for increasing the incentives for private companies to invest in the development of urgently needed new tools and technologies for tackling diseases of poverty, namely an advanced price or purchase commitment (APPC). The lack of effective demand and the resulting poor expected return on investment present a serious deterrent to private sector engagement. The Global Forum for Health Research's 90/10 Report indicated that the public research community also neglects these diseases (2).

A number of studies have addressed the question of how policy-makers and donors might shape and use a package of incentives to encourage companies to invest more in research and development (R&D) for diseases of poverty (3–7). The success of the US Orphan Drug Act (ODA), which combines cost-saving “push” and revenue-enhancing “pull” measures to attract companies to invest in developing products for rare diseases, has set a positive precedent. (The term orphan disease refers to a rare disease affecting fewer than 200 000 Americans.)

Specifically, in the case of orphan diseases in the US, companies with designated orphan products are eligible for tax credits, grants and expedited regulatory approval to reduce the cost of R&D. If successful, their product is guaranteed 7 years of market exclusivity from the date of its approval, increasing the certainty of a return on the company's investment.

Most diseases of poverty technically qualify as orphan diseases in the US and a dozen products that target these diseases have been approved under the ODA (See Table 1) (3). However, market exclusivity has limited value as a pull incentive in these instances because of the small number of cases of these diseases that occur in the US and the fact that this measure does not boost the buying power of patients in the low- and middle-income countries who need the product.

In the light of the evidence on the importance of market size for new drug and vaccine research (8–10), policy forums, articles and working groups have discussed different approaches to enhance the expected market for treatments for diseases of poverty. Much attention has focused on the idea of an advanced price or purchase commitment (APPC) (11–15). Under this mechanism, a third party — presumably one or a group of international agencies, foundations and governments of high-income countries — guarantees a company either a preset price for quantities purchased or a minimum currency amount for

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an approved product that meets preset specifications. To inform current efforts under way to turn this theoretical concept into an operational tool, we address key viability issues by examining lessons from three case studies of incentives designed to motivate companies to increase R&D investment, namely, the United Kingdom's policy for a meningitis C vaccine, the US ODA referred to above and the US BioShield programme.

### Three case studies

#### Meningitis C vaccine in the United Kingdom

During the early 1990s the United Kingdom entered into a form of APPC to respond to an increase in the number of cases of meningitis C (16). Three of five companies approached, Wyeth, North American Vaccines (now Baxter Healthcare) and Chiron, responded to the Ministry of Health's call for a new vaccine. The government established no ex-ante legal guarantees that it would buy the vaccine from any of the companies, but all three developed products that were launched in the

United Kingdom and each won some part of the market in the Ministry tender. The success of this project illustrates the importance of non-legal factors in establishing the credibility of any APPC arrangement.

#### The Orphan Drug Act

Experience gained from the ODA about competition to obtain the "prize" of market exclusivity is highly relevant to the discussion of APPCs. The ODA is regarded as being successful at delivering new products for orphan diseases (8). Drugs and biological products have been brought to market for more than 200 indications of orphan diseases since 1983. This compares to 10 in the previous decade — a tenfold increase per decade (17). The ODA example simulates a situation, somewhat analogous to an APPC, in which companies are competing for a prize. In both the ODA and APPC cases, prior to the incentive being offered, the prospect of even one product earning sufficient returns on the company's investment is low.

Table 1. Orphan products for diseases of poverty

Disease	Generic name	Sponsor(s)	Type of sponsor <sup>a</sup>	Designation date	Approval date
<b>Malaria</b>	Artesunate	WHO <sup>b</sup>	Public	Jul. 99	
	Halofantrine	SKB <sup>c</sup>	Large Rx	Nov. 91	Jul. 92
	Mefloquine HC1	HL Roche <sup>d</sup>	Large Rx	Apr. 88	May 89
	Sodium dichloroacetate	Stacpoole	Individual	Nov. 94	
<b>Leishmaniasis</b>	Aminosidine	Kanyok	Individual	Sept. 94	
	Liposomal amphotericin B	Fujisawa USA	Rx	Dec. 96	Aug. 97
<b>Meningitis</b>	Cytarabine liposomal	DepoTech Corp (now Skye Pharma subsidiary)	Biotech	Jun. 93	Apr. 99
	Liposomal amphotericin B	Fujisawa USA	Rx	Dec. 96	Aug. 97
<b>Tuberculosis</b>	Aconiazide	Lincoln Diagnostics	Diagnostics	Jun. 88	
	Aminosalicic acid	Jacobus Pharm. Co	Rx	Feb. 92	Jun. 94
	Aminosidine	Kanyok	Individual	May. 93	
	Rifalazil	PathoGensis	Biotech	Apr. 99	
	Rifampin	HMR <sup>e</sup>	Large Rx	Dec. 85	May 89
	R,I,P <sup>f</sup>	HMR <sup>e</sup>	Large Rx	Dec. 85	May 94
	Rifapentine	HMR <sup>e</sup>	Large Rx	Jun. 95	Jun. 98
Thalidomide	Celgene Corp	Biotech	Jan. 91		
<b>Trypanosoma</b>	Eflornithine HCl	HMR <sup>e</sup>	Large Rx	Apr. 86	Nov. 90
<b>Hepatitis B</b>	CY-1899	Cytel Corp	Biotech	Mar. 94	
	FIAU	Oclassen Pharm Inc (now Watson Pharm)	Rx	Jul. 92	
	Hepatitis B immune globulin	NABI Biopharm	Biotech	Mar. 95	
	Mono antibody	Protein Design Labs	Biotech	Jun. 91	
	Thymalfasin	SciClone Pharm Inc	Biotech	May. 91	
<b>Leprosy</b>	Clofazimine	Novartis/Ciba-Geigy Corp	Large Rx	Jun. 84	Dec. 86
	Thalidomide	Celgene Corp	Biotech	Jul. 95	Jul. 98
	Thalidomide	Pediatric Pharm	Biotech	Nov. 88	
<b>Totals</b>				<b>25</b>	<b>12</b>

<sup>a</sup> Rx in this column means pharmaceutical companies.

<sup>b</sup> WHO = World Health Organization.

<sup>c</sup> SKB = SmithKline Beecham.

<sup>d</sup> HL Roche = Hoffman-La Roche.

<sup>e</sup> HMR = Aventis Pharmaceuticals.

<sup>f</sup> R,I,P = rifampin, izoniazid, pyrazinamide.

Source: updated from reference 3.

## Project BioShield

The US Government recently approved legislation relating to Project BioShield — a package of “push” and “pull” incentives to accelerate the availability of drugs and vaccines to combat bioterrorist threats such as smallpox, anthrax, Ebola virus and plague (18, 19). The major component of this package is funds appropriated for the purchase of designated products. The government will establish a contract with companies to purchase a product for inclusion in the Strategic National Stockpile up to 5 years before the product is expected to be delivered. The reaction of the biopharmaceutical industry to this proposed legislation provides an insight into how companies might respond to an APPC for a drug or vaccine for a disease of poverty.

## Lessons for designing advance price or purchase commitments to tackle diseases of poverty

As international organizations contemplate the design and size of APPCs, we highlight five key elements that need to be taken into account. Lessons learned from the case studies about how these issues affect the power of the incentive are set out in Table 2 and discussed below.

### Credibility

The APPC must offer a credible commitment to covering the total R&D costs, including out-of-pocket costs, opportunity costs and the costs of failures. DiMasi et al. (20) estimated the total cost for development of a drug to average US\$ 802 million, with a 21.5% success rate from entry into phase 1 to market approval, a duration of 10–12 years and an 11% cost of capital. The study by DiMasi et al. related to drugs and no similar work has been done recently for vaccines, but given the large number of patients required for participation in vaccine trials and the manufacturing costs, the average cost of development is unlikely to be lower than that for a new drug. There is evidence that orphan drugs have been developed at much lower cost (17) in part because of the small size and number of clinical trials (21). Some studies have presented scenarios under which the costs for developing a drug or vaccine for a neglected disease may also be lower (22).

Companies must believe that a promise made now will still hold when their product finally reaches the market, potentially more than a decade later. The meningitis C case, in the United Kingdom, where no legal contract was used, highlights the importance of confidence-building measures and a positive track record in establishing credibility. Key measures that helped reassure companies that the United Kingdom Ministry of Health was a credible partner included:

- a good track record in generating and maintaining political support for the purchase of new vaccines;
- accurate epidemiology of the disease with evidence from the Public Health Laboratory Service (PHLS) and evidence to make the case that the vaccine would deliver good value for money. (It was estimated that a successful meningitis C vaccine would cost some UK£ 1400 per disability-free year achieved. This was a good buy compared to many existing interventions that the health-care system was spending money on, and increased the likelihood of purchase proceeding.);
- repeated public statements (by government and public health professionals) reinforced by positive messages in private discussions;

- a good reputation for delivery in previous vaccination campaigns, to doctors and nurses in surgeries and schools, and supply-chain management skills in the ministry vaccines group;
- assistance from the ministry to complete phase 2 trials. The provision of money in advance (UK£ 1.5 million to the PHLS to do R&D) helped the manufacturers do their work, but also reinforced other signals that the Government of the United Kingdom was committed to getting a product to market.

There is no precedent for APPCs for drugs and vaccines against diseases of poverty and the global health community's track record for purchasing and supporting existing quality products is mixed at best. It will take time to build a credible reputation with the private sector for fulfilling promises and maintaining policies and support. In this environment, it may be essential to have legally binding arrangements to attract companies' attention. The Pull Working Group at the Center for Global Development (11) has demonstrated that a legally binding contract can be drafted (23), but in the absence of supporting evidence, it is difficult to predict whether a legal contract would be sufficient to establish credibility.

The ODA case demonstrates that a perceived change in policy can generate credibility concerns. There are a number of ways in which the strength of the market exclusivity incentive can be undermined (24). The most important of these is when a subsequent entrant successfully demonstrates that their product is clinically superior to that of the first entrant. Technically superior products were eligible for consideration and approval under the ODA, but a precedent was only set in 1996 when the US Food and Drug Administration approved, and courts upheld, a second drug being established as an orphan product for the same indication on safety grounds. At this point industry commentators began to express concerns about the predictability and certainty of the exclusivity provision (25). Evidence to show that these concerns have resulted in any lessening of industry interest and fewer orphan designations is limited. But for a new policy with no track record, such as the APPC, the incentive must be perceived as credible. Companies will not wish to worry that the rules of the game might change over time. For example, how the programme would deal with a second superior product must be clearly stated in advance.

### Setting the specification

The agents of the APPC must clearly specify what kind of product they will pay for and what milestones the company producing the product must achieve to win the contract. In the cases of the meningitis C vaccine in the United Kingdom and the US ODA, the company was granted the prize upon receipt of approval from the national regulatory authority. In the case of BioShield it is unclear what milestone needs to be reached as the companies concerned may not be able to license their products and many cannot be tested in humans.

For a drug or vaccine against a disease of poverty, given that the focus on health impact is *delivered and used* products, not just *approved* ones, the product specifications may go beyond efficacy and safety to include characteristics specific to particular regions such as cost, treatment regime (duration and number of doses) and delivery mechanisms. The contract may specify receipt of the prize at the time of regulatory approval or go further and require that the company ensure delivery of the

Table 2. Design characteristics of case study schemes

Design issue	Meningitis C, United Kingdom	Orphan Drug Act, United States	BioShield
<b>Credibility</b>	<ul style="list-style-type: none"> <li>no advance legal contract</li> <li>continued dialogue</li> <li>scientific/political backing</li> <li>high public profile</li> <li>track record on delivery</li> <li>help with trials and licensing</li> </ul>	<ul style="list-style-type: none"> <li>7 year market exclusivity except for               <ul style="list-style-type: none"> <li>rival indications</li> <li>off-label use</li> <li>“different” products</li> <li>“clinically superior” products</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>buy up to 5 years pre-launch</li> <li>appropriations to be protected<sup>a</sup></li> </ul>
<b>Setting the price</b>	<ul style="list-style-type: none"> <li>competitive tendering</li> <li>small market but potential outside UK</li> <li>scientific certainty</li> <li>no phase 3 trials</li> </ul>	<ul style="list-style-type: none"> <li>third-party payer market</li> <li>evidence of skewed returns</li> </ul>	<ul style="list-style-type: none"> <li>scientific certainty unclear</li> <li>basis for price negotiations unclear</li> <li>limited nongovernment market</li> </ul>
<b>Specification</b>	<ul style="list-style-type: none"> <li>marketing authorization required</li> </ul>	<ul style="list-style-type: none"> <li>marketing authorization required</li> </ul>	<ul style="list-style-type: none"> <li>can be unlicensed</li> <li>specification set by government</li> </ul>
<b>Subsequent entrants</b>	<ul style="list-style-type: none"> <li>several companies approached</li> <li>competitive tendering process</li> <li>all three bidders got business</li> </ul>	<ul style="list-style-type: none"> <li>market exclusivity for first licensee</li> <li>exceptions as above</li> </ul>	<ul style="list-style-type: none"> <li>contracts are company-specific</li> <li>government decides on number of contracts/entrants</li> </ul>
<b>Ensuring use</b>	<ul style="list-style-type: none"> <li>efficient delivery network in schools and surgeries</li> </ul>	<ul style="list-style-type: none"> <li>efficient delivery network</li> </ul>	<ul style="list-style-type: none"> <li>strategic stockpile</li> </ul>

<sup>a</sup> A device in legislation that is designed to prevent Congress changing its mind and stopping the funding. This should mean that companies can do work in the expectation that they will receive payment.

product (11). The agent could offer a range of prices, depending on what the company develops and delivers, effectively awarding a bonus for products that exceed specifications (15).

### Getting the price right

Perhaps the most difficult challenge is that of setting price and volume in advance (26). Too high a price would result in a waste of public finances, but too low a price may result in no company response at all.

Drugs are a risky business and sales are highly skewed (27). Seventy per cent of drugs do not recover the average cost of R&D; the 30% that do so gain significant profit margins for the company that developed them. In the case of the APPC, the price must provide an expectation of revenues that cover the expected costs, including those of failures, and provide a return on R&D investment should the company succeed. Expected revenues will depend, in turn, on expected volumes, the price offered and the probability of winning the APPC. To set the price, the agent must have some understanding of the state of the science and the regulatory process faced by participating companies (hence of expected costs and failure rates), and take a position on the number of entrants it wishes to see undertake the R&D.

An analysis of the societal benefit of the drug or vaccine, including estimates of the monetary value of the health gain, should inform the upper limit to price. Glennerster & Kremer (28) used a base case of US\$ 25 per disability-adjusted life year (DALY) and concluded that vaccines for human immunodeficiency virus/acquired immunodeficiency syndrome, tuberculosis and malaria would be cost-effective at this valuation. Modelling work for the Pull Mechanisms Working Group (11) found a price for a malaria vaccine that could deliver a cost of less than US\$ 20 per disability-adjusted life year (DALY) saved and provide revenue for a company that was in line with that from existing commercial products.

Price setting will also reflect decisions about how to deal with second and third products. If only one product is going to

be purchased, as in a winner-takes-all strategy, the companies' perception of failure risk will be higher and they must therefore be offered a higher price as a potential reward for undertaking the work. If more than one product will be considered, the price offered might be lower.

The price could also change over time. For example, a higher price that covers the cost of R&D could be offered for a pre-specified number of years followed by a lower price that covers only the continued costs of manufacturing and distribution.

In the meningitis C case the Government of the United Kingdom employed competitive tendering in an environment in which bidders expected (and offered) prices to recover the costs of R&D — an environment not likely to be replicated in the case of drugs or vaccines for diseases of poverty. In the ODA case, the company is free to set the price knowing that the volume is made relatively certain by the exclusivity incentive but is limited, at least for the orphan indication for their product. It is unclear how prices will be negotiated under BioShield. It is this lack of clarity combined with the precedent of the US Government threatening to take a compulsory licence for Bayer's Cipro in the wake of the anthrax scare in 2002, among other things, that has discouraged companies from actively supporting the legislation (29).

### Provisions for second and third entrants

Given the scientific challenges and the unlikelihood that the first product to market will meet all of the needs of the targeted patients, even if it meets the product specifications, the APPC should be designed to encourage competition in R&D and to reward subsequent products, while recognizing the impact that this decision would have on incentives. If the APPC does not allow the R&D costs of subsequent entrants to be recovered then the rewards for competing are reduced. On the other hand, if the first to market risks being displaced, incentives may also be compromised.

The United Kingdom Ministry of Health was able to interest three companies in bidding for the relatively small domestic market for a meningitis C vaccine because the development costs were relatively low (the technology had already been developed for other disease applications and the government helped fund some of the clinical trials) and information about markets outside the United Kingdom was available. Under BioShield the US Government has yet to decide on and make public its policy for dealing with subsequent entrants.

Analysis of the ODA experience points to competition in a few cases. On updating Shulman & Manocchia's study (25), we found that for the 187 orphan drugs approved in the period 1983–2002 only 48 (25%) of all the products were in orphan disease areas with more than one product. In less than half of these cases, 21 products, there were competing products designated for the *same* orphan indication — i.e. head-to-head competition for market exclusivity.

Assuming APPCs can support more than one entrant at prices that are socially cost-effective, then the APPC should be structured to allow for more than one winner. However, there could also be a special benefit offered for being first. This could take the form of the price falling over time (i.e. later entrants are rewarded with a lower price) and/or of the APPC requiring subsequent entrants to provide a superior product (as in the ODA case).

The terms of eligibility to win the APPC could require that companies provide upfront disclosure of their intent to undertake research. With this information, the agent and the other companies will know which and how many companies are in the field.

### Ensuring use

Well-organized systems for regulation, procurement and distribution exist for vaccines in the United Kingdom and for orphan drugs in the US. In the case of BioShield, there are precedents for establishing stockpiles of products, a model which the government plans to employ for future products to be used to combat bioterrorism.

In the case of products for tackling diseases of poverty, however, significant obstacles related to political, logistical and capacity issues stand in the way of ensuring that any products that companies develop, and that agents agree to procure, reach and are used by the targeted patients. Given that the ultimate goal of the APPC agents is to reduce the disease burden (i.e. have a health impact) should they offer to buy an approved or a delivered product?

If the APPC is set up such that the company is offered only a price, that company's reward will depend on its ability to secure demand. That is, the company earns money only if it is able to find governments or patients willing to take the product (or accept funds from the procurer to buy the product) (11). Some researchers have gone as far as proposing a co-payment scheme where the agent provides only a top-up on a marginal cost price that the countries and/or patients are committed to paying (15). Companies are unlikely to want to bear the burden of marketing these products in regions and through systems they know little about. So linking their reward to what they are able to sell is likely to dramatically weaken the incentive. That said, the agent cannot be seen to be paying a company for products that sit on a shelf or in a warehouse. A focused effort is required that includes the agent, the company and other global and local stakeholders, and works with countries in advance of

product approval to ensure that the countries are prepared to take up products approved for purchase.

### Achieving a balance between push and pull incentives

In all three of the case studies discussed above, push, or cost-reducing, measures have proven to be an essential complement to the pull measures. This is especially, but not exclusively, the case where small companies have been involved. Push helps reduce the company's risks and upfront costs and arguably might provide the agent with more control over the direction and pace of the product's development, depending on how it structures milestones and monitors progress.

But a move away from a pure APPC to include interim reimbursement of cost or staged payments for achieving intermediate development goals raises a more fundamental problem. The agent has to recognize the high failure rates. It will be paying for intermediate R&D outputs, many of which will not lead to the successful development of a drug or vaccine. The agent will also be in the position of having to select winners — a capability that the donor organizations may or may not have. Assuming that a well-structured APPC will provide companies with enough incentive to undertake (and use internal resources to pay for) product development, it may be more efficient to use pull incentives and let the companies decide how best to allocate the internal resources to ensure an effective outcome. Organizations, such as public–private partnerships, which specialize in research on diseases of poverty, could complement the APPCs, providing companies with disease, agency, and country-specific expertise, guidance and capacities that they might not have in-house (30).

### Conclusions

APPCs are, in principle, high-powered incentives to develop drugs and vaccines for diseases of poverty assuming that the design issues highlighted in this article can be addressed. They target the market uncertainties explicitly and could require less agent intervention in product development than is required by push measures.

Extensive *ex-ante* analysis, including interviews with relevant parties is useful and has taken place. It may be time to start learning-by-doing by taking the more radical step of establishing an APPC, and seeing what happens. The risk profile for testing the idea (from the standpoint of the agent) for particular diseases of poverty will vary according to the state of the science, the state of current development work, if any, and the extent of in-house knowledge of disease that the companies already have. Establishing an APPC for diseases with products already at a late stage of development for which the science and economics (i.e. costs and probability of success) are well understood and the time to market (or failure) is relatively short would provide one kind of test. Work to gain participation from recipient countries might also be made easier with a product already “defined” and closer to market. If successful, i.e. if companies respond and develop a product that works and that countries are willing to use, the launch of the first APPC scheme could be combined with the launch of plans to establish APPCs for diseases and products where science and development efforts are at an earlier stage. ■

**Conflicts of interest:** none declared.

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## Résumé

### Prix garantis ou engagements d'achat destinés à créer des marchés pour les traitements des maladies de la pauvreté : leçons tirées de trois politiques

Le monde a besoin de nouveaux médicaments et de nouveaux vaccins pour s'attaquer aux maladies de la pauvreté dans les pays à revenus faibles et moyens. Le manque de demande ou de marché réels pour ces produits se traduit par des investissements en recherche et développement insuffisants pour satisfaire les besoins. De nombreuses personnes ont préconisé des incitations consistant à réduire les prix (stratégie pousser) ou à renforcer le marché (stratégie tirer) pour faire face à cette difficulté. Le financement par des organismes internationaux ou par des gouvernements de prix garantis ou d'engagements d'achat offre une issue à cette problématique. Le présent article examine les problèmes de conception des stratégies de prix garantis et d'engagements

d'achat pour les médicaments et les vaccins destinés à combattre les maladies de la pauvreté en s'appuyant sur les expériences et les leçons tirées de trois études de cas : l'introduction du vaccin contre la méningite C au Royaume-Uni, la Loi sur les médicaments orphelins (ODA) aux États-Unis d'Amérique et le projet américain contre les actions de bioterrorisme récemment adopté (« Bouclier biologique »). La principale conclusion des auteurs est que les prix garantis et les engagements d'achat peuvent constituer un outil puissant, qui devrait être mis à l'essai. On ne pourra déterminer comment organiser et concevoir correctement ces incitations qu'en engageant le processus conduisant à leur mise en place.

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## Resumen

### Precios garantizados o compromisos de compra como mecanismos de creación de mercados para los tratamientos de las enfermedades de la pobreza: lecciones de tres políticas

Se necesitan nuevos medicamentos y vacunas para abordar las enfermedades asociadas a la pobreza en los países de ingresos bajos y medios. Debido a la falta de una demanda o un mercado efectivos para estos productos, las inversiones en investigación y desarrollo orientadas a cubrir las necesidades de los mismos son insuficientes. Muchos expertos han preconizado incentivos de reducción de costos (impulsores) y de mejora de los mercados (atractores) para abordar este problema. Los precios garantizados y los compromisos de compra (PGCC) financiados por organismos internacionales y gobiernos permitirían avanzar en esa línea. En este artículo se analizan diversos aspectos del diseño de los PGCC

para los medicamentos y vacunas destinados a las enfermedades asociadas a la pobreza, aprovechando para ello la experiencia y las lecciones de tres estudios de casos: la introducción de la vacuna contra la meningitis C en el Reino Unido; la Ley de Medicamentos Huérfanos de los Estados Unidos de América (EE.UU.); y el Proyecto BioShield de los EE.UU., una iniciativa legislativa reciente contra el bioterrorismo. Nuestra principal conclusión es que los PGCC encierran muchas posibilidades para convertirse en un poderoso instrumento y deberían ser ensayados. La estructura y el diseño adecuados sólo podrán determinarse tomando las medidas necesarias para poner en marcha un sistema de ese tipo.

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## References

1. Nwaka S, Ridley R. Virtual drug discovery and development for neglected diseases through public private partnerships. *Nature Reviews Drug Discovery* 2003;2:919-28.
2. Global Forum for Health Research. *10/90 Report on health research, 2003–2004*. Geneva: Global Forum for Health Research; 2004.
3. Kettler H. *Narrowing the gap between provision and need for medicines in developing countries*. London: Office of Health Economics; 2000.
4. WHO–IFPMA Round Table: WHO/Industry Drug Development Working Party. *Working paper on priority infectious diseases requiring additional R&D*. Geneva: World Health Organization; 2001.
5. UK PIU (Performance and Innovation Unit). *Tackling the diseases of poverty: meeting the Okinawa/millennium targets for HIV/AIDS, tuberculosis and malaria*. London: UK Cabinet Office; 2001. Available from: <http://www.cabinet-office.gov.uk/innovation/healthreport/default.htm>
6. Kremer M, Glennerster R. *Strong medicine: creating incentives for pharmaceutical research on neglected diseases*. Princeton (NJ) Princeton University Press; 2004.

7. Milne C, Kaitin K, Ronchi E. *Orphan drug laws in Europe and the US: incentives for the research and development of medicines for the diseases of poverty*. Geneva: Commission on Macroeconomics and Health; 2001. CMH Working Paper Series, Paper No. WG2: 9.
8. Lichtenberg FR, Walsfogel J. *Does misery love company? Evidence from pharmaceutical markets before and after the Orphan Drug Act*. Cambridge (MA): National Bureau of Economic Research; 2003. Working Paper 9750.
9. Acemoglu D, Linn J. *Market size in innovation: theory and evidence from the pharmaceutical industry*. Cambridge (MA): Massachusetts Institute of Technology; 2003. Massachusetts Institute of Technology, Department of Economics Working Paper Series, Working Paper 03-33.
10. Finkelstein A. *Health policy and technological change: evidence from the vaccine industry*. Cambridge (MA): National Bureau of Economic Research; 2003. NBER Working Paper No. 9460.
11. Pull Mechanisms Working Group. *Making markets for vaccines. A practical plan to spark innovations for global health*. Consultation draft report of the Working Group. Washington, DC: Center for Global Development; 2004.
12. Farlow A. *An analysis of the problems of R&D finance for vaccines — and an appraisal of advance purchase commitments*. <http://www.economics.ox.ac.uk/members/andrew.farlow/VaccineRD.pdf>, April 2004.
13. Glennerster R, Kremer M. A better way to spur medical research and development: the purchase precommitment as a supplement to patents and government-funded research. *Regulation* 2001;23:34-9.
14. Kremer M. *Creating markets for new vaccines. Part I. Rationale*. Cambridge (MA): National Bureau of Economic Research; 2000. NBER Working Paper No. 7716.
15. Kremer M. *Creating markets for new vaccines. Part II. Design issues*. Cambridge (MA): National Bureau of Economic Research; 2000. NBER Working Paper No. 7717.
16. Comptroller and Auditor General. *Modern policy-making: ensuring policies deliver value for money*. In: *Report by the Comptroller and Auditor General HC 289 Session 2001-2002*. London: National Audit Office; 2001.
17. Grabowski H. Increasing R&D incentives for neglected diseases: lessons from the Orphan Drug Act. In: Maskus KE, Reichman JH, editors. *International public goods and transfer of technology under a globalized intellectual property regime*. Cambridge: Cambridge University Press; 2004.
18. Gottron F. *Project BioShield: side by side comparisons of House and Senate passed versions, Congressional Research Service Report for Congress*. Washington, DC: Congressional Research Service, Library of Congress; 2004.
19. Gottron F. *Project BioShield. CRS Report for Congress*. Washington, DC: Congressional Research Service, Library of Congress; 2004.
20. Di Masi JA, Hansen RW, Grabowski HG. The price of innovation: new estimates of drug development costs. *Journal of Health Economics* 2003;22:151-85.
21. Reichert JM. Clinical development of therapeutic medicines: a biopharmaceutical versus pharmaceutical product comparison. *Drug Information Journal* 2001;35:337-46.
22. Towse A, Jamison D. *The economics of pharmaceutical R&D for key LDC diseases. Working Paper*. London: Office of Health Economics; 2003.
23. Morantz AD, Sloane RD. *Vaccine purchase-commitment contract: legal strategies for ensuring enforceability*. Cambridge (MA): Harvard University; 2001.
24. Milne C. *Orphan drugs: trends, market forces, and future directions*. Waltham (MA): Decision Resources, Inc; 2001.
25. Shulman S, Manocchia M. The US Orphan Drug Programme 1983–1995. *Pharmacoeconomics* 1997;12:312-26.
26. Laffont J-J, Tirole J. *A theory of incentives in procurement and regulation*. Cambridge (MA): The MIT Press; 1993.
27. Grabowski H, Vernon J, Di Masi J. Returns on research and development for 1990s new drug introductions. *Pharmacoeconomics* 2002;20 Suppl 3:11-29.
28. Glennerster R, Kremer M. *A vaccine purchase commitment: preliminary cost-effectiveness estimates and pricing guidelines*. 2001. Available at: <http://post.economics.harvard.edu/faculty/kremer/papers/vpccost8.pdf>
29. Kerber R. Tech firms wary on biodefense. *Boston Globe*. June 18 2004.
30. Kettler H, Towse A. *Public private partnerships for research and development: medicines and vaccines for diseases of poverty*. London: Office of Health Economics; 2002.